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EXAMPLE 16***Infection of HepG2 cells with recombinant HBV expressing baculovirus***

HepG2 cells were seeded at approximately 20-40% confluency and then were grown for
5 16-24 hours before infection. On the day of infection, triplicate plates of cells were
trypsinized, and viable cell number was determined with a hemocytometer using Trypan
blue exclusion. Average cell counts were calculated and used to determine the volume of
high-titer viral stock necessary to infect cells at the indicated moi. HepG2 cells were
washed one time with serum-free MEM to remove traces of serum. Baculovirus was
10 diluted into MEM without serum to achieve the appropriate moi using volumes of 1.0, 0.5,
and 0.25 ml to infect 100-mm, 60 mm, and 35-mm dishes, respectively. Baculovirus was
adsorbed to HepG2 cells for one hour at 37°C with gentle rocking every 15 minutes to
ensure that the inoculum was evenly distributed. The inoculum was then aspirated and
HepG2 cells were washed two times with phosphate-buffered saline and refed MEM-FBS
15 with or without various concentrations of agents.

EXAMPLE 17***Detection of intracellular replicative intermediates***

20 HBV core particles were isolated from the-cytoplasmic fraction of HepG2 cells lysed in
0.5% w/v NP-40. Cytoplasmic extracts were adjusted to 10 mmol/l McC12 and
unprotected DNA was removed by an incubation to 500 g/ml Proteinase K for 1.5 hours at
37°C. HBV DNA in the samples were then extracted using commercial DNA extraction
kits such as Qiagen (DNA extraction) or in-house methods using sequential phenol and
25 chloroform extractions, and the nucleic acids were recovered by ethanol precipitation.
Nucleic acids were resuspended in 50 µl /l TE (10 mmol/l Tris, 1 mmol/l
ethylenediaminetetraacetic acid), normalized by OD260, and digested with 100 g/ml
RNase (Boehringer Mannheim, Indianapolis, IN) for one hour at 37°C before analysis by
real-time PCR or electrophoresis and Southern blotting. After southern blot analysis a
30 BioRad GS-670 imaging densitometer and the Molecular Analyst software (BioRad,
Hercules California) was used to analyze suitable exposures of Southern blots.

Densitometry data was fitted to logistic dose response curves using the TableCurve 2D software package from Jandel Scientific. Logistic dose response equations were used to calculate IC₅₀ and IC₉₀ values and co-efficients of variation.

5

EXAMPLE 18

Real-time PCR

For the real-time PCR based assay for HBV, HBV DNA was extracted from 200 µl of serum using the QIAamp DNA Mini Kit according to the manufacturer's instructions (QIAGEN GmbH, Hildens, Germany). Primers and a molecular beacon were designed for conserved nucleic acid sequences within the precore domain of the HBV genome to amplify and detect a 216-nucleotide product. Amplification was performed in a 50-µl reaction mixture containing 1.0 Taqman buffer A (Applied Biosystems, Foster City, CA), 3.0 mM MgCl₂, 0.4 pmol of each primer per µL, forward primer, PC1 (5'-GGGAGGAGATTAGGTAA-3' [SEQ ID NO:12]) and reverse primer, PC2 (5'-GGCAAAAACGAGAGTAACTC-3' [SEQ ID NO:13]), 0.4 pmol of the HBV-specific molecular beacon per µL, (5'-FAM-CGCGTCCTACTGTTCAAGCCTCCAAGCTGTGACGCG-DABCYL-3' [SEQ ID NO:14]; where FAM represents fluorophore 6-carboxyfluorescein and DABCYL, 4-dimethylaminophenylazobenzoic acid, a quenching chromophore) and 1.25U of AmpliTaq Gold DNA polymerase (Perkin-Elmer). PCR was performed using the ABI PRISM 7700 spectrofluorometric thermocycler (Applied Biosystems). The PCR program consisted of an initial cycle (95°C for 10 minutes) followed by 45 amplification cycles (94°C for 15 secs, 50°C for 30 secs, 72°C for 30 secs). The instrument detected and recorded the fluorescence spectrum of each reaction tube during the annealing phase.

An external standard was constructed by ligation of a 1.3 kB wild-type HBV plasmid (genotype D) into the pBlueBac plasmid vector (Hershey Medical Center, Hershey, PA). Quantification of the DNA concentration of the plasmid was determined by spectrophotometry. Duplicates of serial 10-fold dilutions of the plasmid ranging from 10⁸ copies/ml to 100 copies/ml were included in each run in order to generate a standard curve.

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The copy number in each experimental reaction was determined by interpolation of the derived threshold cycle (C_T).

EXAMPLE 19

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ADV treatments

ADV was resuspended in sterile water, aliquoted, and frozen at -20°C to avoid repeated freezing and thawing of the drug. Medium containing ADV was prepared daily as needed using fresh aliquots of 3TC. In experiments in which ADV treatment was initiated after
10 viral infection, HepG2 cells were exposed to the indicated concentration of ADV immediately after infection with HBV baculovirus. In experiments utilizing pretreatment with ADV, cells were fed medium containing ADV 16 hours prior to HBV baculovirus infection, HBV baculovirus infection was also carried out in medium containing ADV, and cells were refed fresh medium containing ADV immediately after completion of the
15 infection and washing procedures.

EXAMPLE 20

Antiviral testing performed with wild-type and HBV/baculovirus encoding rtA181T/N236T/N238D and rtN236T/N236D

20

The *in vitro* antiviral drug cross-resistance testing of the HBV mutants is shown in Table 18. The laboratory reference strain of HBV (genotype D subtype ayw) containing the introduced D domain mutations demonstrated increased IC_{50} values against ADV (Table 18). The rt N236T/N238D mutation was associated with a twenty-three fold increase in
25 IC_{50} against ADV. This was reduced to a five-fold increase when the rtA181T was also present and this triple HBV polymerase mutant was resistant to LMV.

TABLE 4 Clinical, virological and HBV sequencing data summary for Patient A while on open label ADV.

5

Days post-ADV treatment	HBV DNA copies/ml (pg/ml)	ALT IU/L	Treatment protocol	Key polymerase mutations detected by sequencing ¹
-230	1.7 10 ⁶ (61)	67 U/L	pre-therapy	rtT/N128T/N rtQ/H/R215Q/stop
875			ADV recommenced	
904	1.55 x 10 ⁶			
932	2.97 x 10 ⁶			
959	1.76 x 10 ⁶			
983	1.64 x 10 ⁶	65	end ADV	rtT128N rtY135C

¹ Nomenclature according to Stuyver *et al.*, 2001, *supra*

TABLE 5 Summary of HBV mutations in patient A treated with ADV

Sample name	Days post-ADV treatment	Genotype	Polymerase*	Surface
ILA1	-230	D	rtA/S21A/S rtT/N128T/N** rtQ/H/R215Q/stop	sP120P/T sI208I/L
ILA2	904	D	rtA/S21S rtF122L rtR126H rtT/N128T/N rtQ130P rtN131D rtQstop/215Q rtH248N	sP/T120P sT125M sI/I208I/L
ILA3	932	D	rtA/S21S rtF122L rtR126H rtT/N128T/N rtQ130P rtN131D rtQstop/215Q rtH248N	sP/T120P sT125M sI/I208I/L
ILA4	983	D	rtS21A rtL122F rtN124H rtH126R rtT128N rtP130Q rtD131N rtY135C	sP120T sM125T sT127A

* Nomenclature according to Stuyver *et al.*, 2001, *supra*.

5 ** Mutations in bold have not been detected in reference HBV genotypes, mutations not in bold are changes from the previous sample that are present in reference genotypes.

TABLE 6 Clinical, virological and HBV sequencing data summary for Patient B while on open label ADV.

Days post-ADV treatment	HBV DN copies/ml (pg/ml)	ALT IU/L	Treatment protocol	Key polymerase mutations detected by sequencing ¹
-867(S0)	183	298	pre-therapy	rtN/S/T/I/V53D rtV153G rtQ/E215S rtN248H
-8(S6)	955	427	pre-ADV on LMV	rtI/L80L rtY126Q rtL180M rtS202G rtI204V
76(S8)	not detected	150	on ADV (20 mg) and LMV	rtN/S/T/I/V53D rtY126Q rtL180M rtS202G rtI204V
637(S12)	not detected	36	on ADV (5 mg) and LMV	rtN/S/T/I/V53D rtY126Q rtL180M rtS202G rtI204V
872(S15)	not detected	67	on ADV (5 mg) and LMV	rtN/S/T/I/V53D rtY126Q rtL180M rtS202G rtI204V rtI235I/M

5 ¹ Nomenclature according to Stuyver *et al.*, 2001, *supra*

TABLE 7 Summary of HBV mutations in Patient B treated with ADV

Sample name	Days post-ADV treatment	Genotype	Polymerase*	Surface
S0	-867	D	rtN/S/T/I/V53D rtV153G rtQ/E215S rtN248H	sM/K/L133T sF134V sS207R sL21V/L
S6	-8	D	rtI/L80L rtY126Q rtL180M rtS202G rtI204V	sT118R sM133T sF134V sI195M sS207R
S8	76	D	rtN/S/T/I/V53D rtY126Q rtL180M rtS202G rtI204V	sT118R sM133T sF134V sI195M sS207R
S12	637	D	rtN/S/T/I/V53D rtY126Q rtL180M rtS202G I204V	sT118R sM133T sF134V sI195M sS207R
S15	872	D	rtN/S/T/I/V53D rtY126Q rtL180M rtS202G rtI204V rtI235I/M	sT118R sM133T sF134V sI195M sS207R sY225Y/C

5 * Nomenclature according to Stuyver *et al.*, 2001, *supra*

** Mutations in bold have not been detected in reference HBV genotypes, mutations not in bold are changes from the previous sample that are present in reference genotypes.

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TABLE 8 Clinical, virological and HBV sequencing data summary for Patient C while on open label ADV.

Days post-ADV treatment	HBV DNA copies/ml (pg/ml)	ALT IU/L	Treatment protocol	Key polymerase mutations detected by sequencing ¹
-26	2×10^7		pre-therapy	rtN53D rtS116P rtD/N/S134V rtN238D
0		240	ADV commenced clinical trial	
29		160		
630		407		
668			Open label ADV	
701	1.5×10^7	226		
730	3.7×10^6	361		rtN53D rtS116P rtF151S/T rtA181T rtN236T rtN238D
738		517		
739			end ADV, start LMV	

5 ¹ Nomenclature according to Stuyver *et al.*, 2001, *supra*

TABLE 9 Summary of HBV mutations in Patient C treated with ADV

Sample name	Days post-ADV treatment	Genotype	Polymerase*	Surface
DRJ1299	-26	D	rtN53D** rtY54H rtS57P rtL91I rtS116P rtF122L rtY124H rtD/N/S134V rtK212R rtL217R rtS219A rtN238D	T126S S204G L209V S210R
DRJ1	730	D	rtN53D rtY54H rtS57P rtL91I rtS116P rtF122L rtY124H rtV134D rtY141Y/F rtL145M rtF151T/F rtA181T rtK212R rtL217R rtS219A rtN236T rtN238D	sS126T sM133L/M sS143S/T sD144A sG145A sW172Stop

* Nomenclature according to Stuyver *et al.*, 2001, *supra*.

5 ** Mutations in bold have not been detected in reference HBV genotypes, mutations not in bold are changes from the previous sample that are present in reference genotypes.

TABLE 10 Summary of HBV mutations in Patient D treated with ADV

Sample Name	Genotype	Polymerase*	Surface
02575908	D	rtS78T rtV84M rtY126C rtV191I rtM204I rtV214A	sN40S sC69stop sM75I sL88P sT118A sW182STOP sW196L sY206H sY225F

* Nomenclature according to Stuyver *et al.*, 2001, *supra*.

5 ** Mutations in bold have not been detected in reference HBV genotypes, mutations not in bold are changes from the previous sample that are present in reference genotypes.

TABLE 11 Summary of HBV mutations in Patient E treated with ADV

Sample Name	Genotype	Polymerase*	Surface
8123/02	A	rtH90D rtL/F108L 6nt insertion/duplication after codon rt131(aaQ&N)	sI81M sY/S100Y 6nt insertion/ duplication after codon s122 (aaT & K) sP214Q

10 *

Nomenclature according to Stuyver *et al.*, 2001, *supra*.

** Mutations in bold have not been detected in reference HBV genotypes, mutations not in bold are changes from the previous sample that are present in reference genotypes.

TABLE 12 Codons where mutations occur following exposure to nucleoside or nucleotide analogs

Region/ Domain	Original amino acid in reverse transcriptase (rt) and codon position	Nucleotide				
prior to F	K32	AAG	AAA			
	N33	AAT				
	P34	CCT				
	H35	CAC				
	T37	ACC				
F TO A	P59	CCA				
	K60	AAA				
	F61	TTC				
	A62	GCA				
	V63	GTC				
A	D83	GAT				
	V84	GTG				
	S85	TCT				
	A86	GCG				
	Y89	TAT				
	H90	CAT				
	I/L91	ATT	CTT			
B	P177	CCG				
	F178	TTT				
	L179	CTC				
	L180	CTG				
	A181	TTG				
	Q182	CAG				
	F183	TTT				
	T184	ACT				
C	Y203	TAT				
	M204	ATG				
D	L235	TTG	TTA			
	N236	AAC	AAT			
	T237	ACT	ACC			
	P237	CCT	CCC			
	N238	AAT	AAC			
	H238	CAC				
	A238	GCT				
	S238	TCT				
	Q238	CAG				

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Region/ Domain	Original amino acid in reverse transcriptase (rt) and codon position	Nucleotide				
	K239	AAA	AAG			
E	L247	CTT	TTA	CTA	CTC	CTG
	N248	AAC	AAT			
	H248	CAT	CAC			
	F249	TTC	TTT			
	M250	ATG				
	G251	GGT	GGA	GGC	GGG	
	V251	GTC				

TABLE 13 Target amino acid sites in rt with codons and mutations leading to amino acid changes.



Title	Codon	Amino Acid	Codon	Amino Acid	Codon	Amino Acid
K32	AAG	Lys	AAG	Lys	GAG	Glu
N33	AAT	Asn	AAT	Asn	GAT	Asp
P34	CCT	Pro	ACT	Thr	GCT	Ala
H35	CAC	His	AAC	Asn	GAC	Asp
T37	ACC	Thr	ACC	Thr	GCC	Ala
P59	CCA	Pro	ACA	Thr	GCA	Ala
K60	AAA	Lys	AAA	Lys	GAA	Glu
F61	TTC	Phe	ATC	Ile	GTC	Val
A62	GCA	Ala	ACA	Thr	GCA	Ala
V63	GTC	Val	ATC	Ile	GTC	Val
D83	GAT	Asp	AAT	Asn	GAT	Asp
V84	GTG	Val	ATG	Met	GTG	Val
S85	TCT	Ser	ACT	Thr	GCT	Ala
A86	GCG	Ala	ACG	Thr	GCG	Ala
Y89	TAT	Tyr	AAT	Asn	GAT	Asp
H90	CAT	His	AAT	Asn	GAT	Asp
I/L91	ATT	Ile	ATT	Ile	GTT	Val
P177	CCG	Pro	ACG	Thr	GCG	Ala
F178	TTT	Phe	ATT	Ile	GTT	Val
L179	CTC	Leu	ATC	Ile	GTC	Val
L180	CTG	Leu	ATG	Met	GTG	Val
A181	TTG	Leu	ATG	Met	GTG	Val
Q183	CAG	Gln	AAG	Lys	GAG	Glu
F183	TTT	Phe	ATT	Ile	GTT	Val
T184	ACT	Thr	ACT	Thr	GCT	Ala
Y203	TAT	Tyr	AAT	Asn	GAT	Asp
M204	ATG	Met	ATG	Met	GTG	Val
L235	TTG	Leu	ATG	Met	GTG	Val
N236	AAC	Asn	AAC	Asn	GAC	Asp
T237	ACT	Thr	ACT	Thr	GCT	Ala
P237	CCT	Pro	ACT	Thr	GCT	Ala
N238	AAT	Asn	AAT	Asn	GAT	Asp
H238	CAC	His	AAC	Asn	GAC	Asp
A238	GCT	Ala	ACT	Thr	GCT	Ala
S239	TCT	Ser	ACT	Thr	GCT	Ala
Q238	CAG	Gln	AAG	Lys	GAG	Glu
K239	AAA	Lys	AAA	Lys	GAA	Glu
L247	CTT	Leu	ATT	Ile	GTT	Val
N248	AAC	Asn	AAC	Asn	GAC	Asp
H248	CAT	His	AAT	Asn	GAT	Asp
F249	TTC	Phe	ATC	Ile	GTC	Val
M250	ATG	Met	ATG	Met	GTG	Val
G251	GGT	Gly	AGT	Ser	GGT	Gly
V251	GTC	Val	ATC	Ile	GTC	Val

TABLE 13 continued (II)

Codon	Amino Acid	Codon	Amino Acid	Codon	Amino Acid
CAG	Gln	TAG	Stop	AAG	Lys
CAT	His	TAT	Tyr	AAT	Asn
CCT	Pro	TCT	Ser	CAT	His
CAC	His	TAC	Tyr	CAC	His
CCC	Pro	TCC	Ser	AAC	Asn
CCA	Pro	TCA	Ser	CAA	Gln
CAA	Gln	TAA	Stop	AAA	Lys
CTC	Leu	TTC	Phe	TAC	Tyr
CCA	Pro	TCA	Ser	GAA	Glu
CTC	Leu	TTC	Phe	GAC	Asp
CAT	His	TAT	Tyr	GAT	Asp
CTG	Leu	TTG	Leu	GAG	Glu
CCT	Pro	TCT	Ser	TAT	Tyr
CCG	Pro	TCG	Ser	GAG	Glu
CAT	His	TAT	Tyr	TAT	Tyr
CAT	His	TAT	Tyr	CAT	His
CTT	Leu	TTT	Phe	AAT	Asn
CCG	Pro	TCG	Ser	CAG	Gln
CTT	Leu	TTT	Phe	TAT	Tyr
CTC	Leu	TTC	Phe	CAC	His
CTG	Leu	TTG	Leu	CAG	Gln
CTG	Leu	TTG	Leu	TAG	Stop
CAG	Gln	TAG	Stop	CAG	Gln
CTT	Leu	TTT	Phe	TAT	Tyr
CCT	Pro	TCT	Ser	AAT	Asn
CAT	His	TAT	Tyr	TAT	Tyr
CTG	Leu	TTG	Leu	AAG	Lys
CTG	Leu	TTG	Leu	TAG	Stop
CAC	His	TAC	Tyr	AAC	Asn
CCT	Pro	TCT	Ser	AAT	Asn
CCT	Pro	TCT	Ser	CAT	His
CAT	His	TAT	Tyr	AAT	Asn
CAC	His	TAC	Tyr	CAC	His
CCT	Pro	TCT	Ser	GAT	Asp
CCT	Pro	TCT	Ser	TAT	Tyr
CAG	Gln	TAG	Stop	CAG	Gln
CAA	Gln	TAA	Stop	AAA	Lys
CTT	Leu	TTT	Phe	CAT	His
CAC	His	TAC	Tyr	AAC	Asn
CAT	His	TAT	Tyr	CAT	His
CTC	Leu	TTC	Phe	TAC	Tyr
CTG	Leu	TTG	Leu	AAG	Lys
CGT	Arg	TGT	Cys	GAT	Asp
CTC	Leu	TTC	Phe	GAC	Asp

TABLE 13 continued (III)

Codon	Amino Acid	Codon	Amino Acid	Codon	Amino Acid
AGG	Arg	ACG	Thr	ATG	Met
AGT	Ser	ACT	Thr	ATT	Ile
CGT	Arg	CCT	Pro	CTT	Leu
CGC	Arg	CCC	Pro	CTC	Leu
AGC	Ser	ACC	Thr	ATC	Ile
CGA	Arg	CCA	Pro	CTA	Leu
AGA	Arg	ACA	Thr	ATA	Ile
TGC	Cys	TCC	Ser	TTC	Phe
GGA	Gly	GCA	Ala	GTA	Val
GGC	Gly	GCC	Ala	GTC	Val
GGT	Gly	GCT	Ala	GTT	Val
GGG	Gly	GCG	Ala	GTG	Val
TGT	Cys	TCT	Ser	TTT	Phe
GGG	Gly	GCG	Ala	GTG	Val
TGT	Cys	TCT	Ser	TTT	Phe
CGT	Arg	CCT	Pro	CTT	Leu
AGT	Ser	ACT	Thr	ATT	Ile
CGG	Arg	CCG	Pro	CTG	Leu
TGT	Cys	TCT	Ser	TTT	Phe
CGC	Arg	CCC	Pro	CTC	Leu
CGG	Arg	CCG	Pro	CTG	Leu
TGG	Trp	TCG	Ser	TTG	Leu
CGG	Arg	CCG	Pro	CTG	Leu
TGT	Cys	TCT	Ser	TTT	Phe
AGT	Ser	ACT	Thr	ATT	Ile
TGT	Cys	TCT	Ser	TTT	Phe
AGG	Arg	ACG	Thr	ATG	Met
TGG	Trp	TCG	Ser	TTG	Leu
AGC	Ser	ACC	Thr	ATC	Ile
AGT	Ser	ACT	Thr	ATT	Ile
CGT	Arg	CCT	Pro	CTT	Leu
AGT	Ser	ACT	Thr	ATT	Ile
CGC	Arg	CCC	Pro	CTC	Leu
GGT	Gly	GCT	Ala	GTT	Val
TGT	Cys	TCT	Ser	TTT	Phe
CGG	Arg	CCG	Pro	CTG	Leu
AGA	Arg	ACA	Thr	ATA	Ile
CGT	Arg	CCT	Pro	CTT	Leu
AGC	Ser	ACC	Thr	ATC	Ile
CGT	Arg	CCT	Pro	CTT	Leu
TGC	Cys	TCC	Ser	TTC	Phe
AGG	Arg	ACG	Thr	ATG	Met
GGT	Gly	GCT	Ala	GTT	Val
GGC	Gly	GCC	Ala	GTC	Val

TABLE 13 continued (IV)

Codon	Amino Acid	Codon	Amino Acid	Codon	Amino Acid	Codon	Amino Acid
AAA	Lys	AAG	Lys	AAC	Asn	AAT	Asn
AAA	Lys	AAG	Lys	AAC	Asn	AAT	Asn
CCA	Pro	CCG	Pro	CCC	Pro	CCT	Pro
CAA	Gln	CAG	Gln	CAC	His	CAT	His
ACA	Thr	ACG	Thr	ACC	Thr	ACT	Thr
CCA	Pro	CCG	Pro	CCC	Pro	CCT	Pro
AAA	Lys	AAG	Lys	AAC	Asn	AAT	Asn
TTA	Leu	TTG	Leu	TTC	Phe	TTT	Phe
GCA	Ala	GCG	Ala	GCC	Ala	GCT	Ala
GTA	Val	GTG	Val	GTC	Val	GTT	Val
GAA	Glu	GAG	Glu	GAC	Asp	GAT	Asp
GTA	Val	GTG	Val	GTC	Val	GTT	Val
TCA	Ser	TCG	Ser	TCC	Ser	TCT	Ser
GCA	Ala	GCG	Ala	GCC	Ala	GCT	Ala
TAA	Stop	TAG	Stop	TAC	Tyr	TAT	Tyr
CAA	Gln	CAG	Gln	CAC	His	CAT	His
ATA	Ile	ATG	Met	ATC	Ile	ATT	Ile
CCA	Pro	CCG	Pro	CCC	Pro	CCT	Pro
TTA	Leu	TTG	Leu	TTC	Phe	TTT	Phe
CTA	Leu	CTG	Leu	CTC	Leu	CTT	Leu
CTA	Leu	CTG	Leu	CTC	Leu	CTT	Leu
TTA	Leu	TTG	Leu	TTC	Phe	TTT	Phe
CAA	Gln	CAG	Gln	CAC	His	CAT	His
TTA	Leu	TTG	Leu	TTC	Phe	TTT	Phe
ACA	Thr	ACG	Thr	ACC	Thr	ACT	Thr
TAA	Stop	TAG	Stop	TAC	Tyr	TAT	Tyr
ATA	Ile	ATG	Met	ATC	Ile	ATT	Ile
TTA	Leu	TTG	Leu	TTC	Phe	TTT	Phe
AAA	Lys	AAG	Lys	AAC	Asn	AAT	Asn
ACA	Thr	ACG	Thr	ACC	Thr	ACT	Thr
CCA	Pro	CCG	Pro	CCC	Pro	CCT	Pro
AAA	Lys	AAG	Lys	AAC	Asn	AAT	Asn
CAA	Gln	CAG	Gln	CAC	His	CAT	His
GCA	Ala	GCG	Ala	GCC	Ala	GCT	Ala
TCA	Ser	TCG	Ser	TCC	Ser	TCT	Ser
CAA	Gln	CAG	Gln	CAC	His	CAT	His
AAA	Lys	AAG	Lys	AAC	Asn	AAT	Asn
CTA	Leu	CTG	Leu	CTC	Leu	CTT	Leu
AAA	Lys	AAG	Lys	AAC	Asn	AAT	Asn
CAA	Gln	CAG	Gln	CAC	His	CAT	His
TTA	Leu	TTG	Leu	TTC	Phe	TTT	Phe
ATA	Ile	ATG	Met	ATC	Ile	ATT	Ile
GGA	Gly	GGG	Gly	GGC	Gly	GGT	Gly
GTA	Val	GTG	Val	GTC	Val	GTT	Val

TABLE 14 Amino acid mutations at target sites in rt

Target	Mutation
K32	M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L
N33	D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R
P34	S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F
H35	I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G
T37	W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S
P59	S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F
K60	M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L
F61	P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M
A62	R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V
V63	A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y
D83	C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N
V84	A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y
S85	T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P
A86	R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V
Y89	V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W
H90	I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G
I/L91	K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H
P177	S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F
F178	P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M
L179	K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I
L180	K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I
A181	R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V
Q183	E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C
F183	P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M
T184	W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S
Y203	V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W
M204	F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K
L235	K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I
N236	D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R
T237	W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S
P237	S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F
N238	D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R
H238	I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G
A238	R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V
S239	T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P
Q238	E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C
K239	M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L
L247	K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I
N248	D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R
H248	I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G

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Target	Mutation
F249	P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M
M250	F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K
G251	H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E
V251	A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y

TABLE 15 Summary of HBV mutations in Patient F treated with ADV

Sample Name	Genotype	Polymerase*	Surface
CAP 01564808	A	rtL157L/M rtA181V rtV207I rtN236T	sF83S sL173F sW199L

5

* Nomenclature according to Stuyver *et al.*, 2001, *supra*.

** Mutations in bold have not been detected in reference HBV genotypes, mutations not in bold are changes from the previous sample that are present in reference genotypes.

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TABLE 16 Summary of HBV mutations in Patient G treated with ADV

Sample Name	Genotype	Polymerase*	Surface
KAN 02510355	C	rtL80V rtP109S rtI163V rtM204I rtL229M rtN/H/A/S/Q238K	sI126T sK160R sS174N sA184V sW196L sS210N sF/C220L sY221C

* Nomenclature according to Stuyver *et al.*, 2001, *supra*.

- 5 ** Mutations in bold have not been detected in reference HBV genotypes, mutations not in bold are changes from the previous sample that are present in reference genotypes.

TABLE 17 Summary of HBV mutations in Patient H treated with ADV

Sample Name	Genotype	Polymerase*	Surface
LAV0303	D	rtS78S/T rtN118N/S rtN139N/K rtV142E rtA181A/T rtI204M rtQ/P/S/Stop215Q rtE218K/E rtN238N/H	sC69Stop/C sC76Y sI110V/I sY134N sW172Stop/W sW196Stop sS207R

10

* Nomenclature according to Stuyver *et al.*, 2001, *supra*.

- ** Mutations in bold have not been detected in reference HBV genotypes, mutations not in bold are changes from the previous sample that are present in reference genotypes.

TABLE 18 *In vitro* drug susceptibility of the HBV reference laboratory strain and patient-derived HBV isolate

Mutation	<i>In vitro</i> Susceptibility IC ₅₀ (fold change from wild-type)		
	Real-time PCR	Southern Blot	
	Adefovir	Adefovir	Lamivudine
Wild-type (pPC)	1	1	1
rt N236T/N238D	23	NA ¹	NA ¹
rt A181T/N236T/N238D	5.1	7.3	>100
rt L180M/M204V ²	NT ⁵	0.9	>2500

5 ¹ NA, not analyzed.

² Data from Delaney *et al.*, 2001, *supra*

Those skilled in the art will appreciate that the invention described herein is susceptible to variations and modifications other than those specifically described. It is to be understood
 10 that the invention includes all such variations and modifications. The invention also includes all of the steps, features, compositions and compounds referred to or indicated in this specification, individually or collectively, and any and all combinations of any two or more of said steps or features

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CLAIMS

1. An isolated HBV variant wherein said variant comprises a nucleoside mutation in a gene encoding a DNA polymerase resulting in at least one amino acid addition, substitution and/or deletion to said DNA polymerase and wherein said variant exhibits decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV and/or optionally other nucleoside or nucleotide analogs or other anti-HBV agents or combinations thereof
2. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to ADV.
3. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to both LMV.
4. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to TFV.
5. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to FTC.
6. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to ADV and LMV.
7. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to ADV and TFV.
8. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to LMV and TFV.

9. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to ADV and FTC.
10. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to LMV and FTC.
11. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to TFV and FTC.
12. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to ADV and LMV and TFV.
13. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to ADV and LMV and FTC.
14. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to FTC and LMV and TFV.
15. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to ADV and FTC and TFV.
16. The isolated HBV variant of Claim 1 wherein said variant exhibits decreased sensitivity to ADV and LMV and TFV and FTC.
17. The isolated HBV variant of any one of Claims 1 to 16 wherein said variant exhibits reduced interactivity to an immunological reagent specific to HBsAg.
18. The isolated HBV variant of Claim 1 wherein said variant comprises a mutation in domain F of the HBV DNA polymerase thereby conferring an altered amino acid sequence to the sequence set forth in Formula I [SEQ ID NO:1]:

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FORMULA I

L, X₁, X₂, D, W, G, P, C, X₃, X₄, H, G, X₅, H, X₆, I, R, X₇, P, R, T, P, X₈, R, V, X₉, G, G, V, F, L, V, D, K, N, P, H, N, T, X₁₀, E, S, X₁₁, L, X₁₂, V, D, F, S, Q, F, S, R, G, X₁₃, X₁₄, X₁₅, V, S, W, P, K, F, A, V, P, N, L, X₁₆, S, L, T, N, L, L, S*

wherein:

- X₁ is L or R or I;
- X₂ is E or D;
- X₃ is T or D or A or N or Y;
- X₄ is E or D;
- X₅ is E or K or Q;
- X₆ is H or R or N;
- X₇ is I or T;
- X₈ is A or S;
- X₉ is T or R;
- X₁₀ is A or T or S;
- X₁₁ is R or T;
- X₁₂ is V or G;
- X₁₃ is S or I or T or N or V;
- X₁₄ is T or S or H or Y;
- X₁₅ is R or H or K or Q;
- X₁₆ is Q or P;

and wherein S* is designated as amino acid 74.

19. The isolated HBV variant of Claim 1 wherein said variant comprises a mutation in any one of domains A through E thereby conferring an altered amino acid sequence to the sequence set forth in Formula II [SEQ ID NO:2]:

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FORMULA II

$SX_1LSWLSLDVSAAFYHX_2PLHPAAMPHELLX_3GSSGLX_4RYV$
 $ARLSSX_5SX_6X_7XNX_8QX_9X_{10}XXXXX_{11}LHX_{12}X_{13}CSRX_{14}LYVSLX_{15}$
 $LLYX_{16}TX_{17}GX_{18}KLHLX_{19}X_{20}HPIX_{21}LGFRKX_{22}PMGX_{23}GLSPFL$
 $LAQFTSAIX_{24}X_{25}X_{26}X_{27}X_{28}RAFX_{29}HCX_{30}X_{31}FX_{32}YM^*DDX_{33}VLGA$
 $X_{34}X_{35}X_{36}X_{37}HX_{38}EX_{39}LX_{40}X_{41}X_{42}X_{43}X_{44}X_{45}X_{46}LLX_{47}X_{48}GIHLNPX_{49}K$
 $TKRWGYSLNFMGYX_{50}IG$

wherein:

- X is any amino acid
- X_1 is N or D;
- X_2 is I or P;
- X_3 is I or V;
- X_4 is S or D;
- X_5 is T or N;
- X_6 is R or N;
- X_7 is N or I;
- X_8 is N or Y or H;
- X_9 is H or Y;
- X_{10} is G or R;
- X_{11} is D or N;
- X_{12} is D or N;
- X_{13} is S or Y;
- X_{14} is N or Q;
- X_{15} is L or M;
- X_{16} is K or Q;
- X_{17} is Y or F;
- X_{18} is R or W;

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X₁₉ is Y or L;
X₂₀ is S or A;
X₂₁ is I or V;
X₂₂ is I or L;
X₂₃ is V or G;
X₂₄ is C or L;
X₂₅ is A or S;
X₂₆ is V or M;
X₂₇ is V or T;
X₂₈ is R or C;
X₂₉ is F or P;
X₃₀ is L or V;
X₃₁ is A or V;
X₃₂ is S or A;
X₃₃ is V or L or M;
X₃₄ is K or R;
X₃₅ is S or T;
X₃₆ is V or G;
X₃₇ is Q or E;
X₃₈ is L or S or R;
X₃₉ is S or F;
X₄₀ is F or Y;
X₄₁ is T or A;
X₄₂ is A or S;
X₄₃ is V or I;
X₄₄ is T or C;
X₄₅ is N or S;
X₄₆ is F or V;
X₄₇ is S or D;
X₄₈ is L or V;
X₄₉ is N or Q;

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X₅₀ is V or I; and
M* is amino acid 204;

and wherein the first S is designated as amino acid 75.

20. The isolated HBV variant of Claim 18 or 19 wherein said variant further comprises an altered HBsAg.
21. An isolated HBV variant comprising a mutation in the nucleotide sequence encoding HBsAg resulting in an amino acid addition, substitution and/or deletion in said HBsAg in a region corresponding to the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2 and wherein said variant exhibits decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV and/or optionally other nucleoside or nucleotide analogs or other anti-HBV agents or combinations thereof.
22. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased sensitivity to ADV.
23. The isolated HBV variant of Claim 21 wherein said variants exhibits decreased sensitivity to LMV.
24. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased sensitivity to TFV.
25. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased sensitivity to FTC.
26. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased

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sensitivity to ADV and LMV.

27. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased sensitivity to LMV and TFV.

28. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased sensitivity to ADV and FTC.

29. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased sensitivity to LMV and FTC.

30. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased sensitivity to TFV and FTC.

31. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased sensitivity to ADV and TFV.

32. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased sensitivity to ADV and LMV and TFV.

33. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased sensitivity to ADV and LMV and FTC.

34. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased sensitivity to FTC and LMV and TFV.

35. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased sensitivity to ADV and FTC and TFV. --

36. The isolated HBV variant of Claim 21 wherein said variant exhibits decreased sensitivity to ADV and LMV and TFV and FTC.

37. The isolated HBV variant of Claim 21 wherein an antibody specific for a wild-type HBsAg exhibits a reduced capacity to neutralize said HBV variant and wherein said HBV variant is selected by exposure of a subject to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, in single or combinations or sequential therapy.
38. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtS21A, rtL122F, rtN124H, rtT28N, rtP130Q, rtD131N and rtY135C or a combination thereof or an equivalent mutation.
39. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtN/S/T/I/V53D, rtY126Q, rtL180M, rtS202G, rtI204V and rtI235I/M or a combination thereof or an equivalent mutation.
40. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtN53D, rtY54H, rtS57P, rtL91I, rtS116P, rtF122L, rtY124H, rtV134D, rtY141Y/F, rtL145M, rtF151F/Y, rtA181T, rtK212R, rtL217R, rtS219A, rtN236T and rtN238D or a combination thereof or an equivalent mutation.
41. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtH90D and rtL/F108L or a combination thereof or an equivalent mutation.
42. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtL157L/M, rtA181V and rtV207I or a combination thereof or an equivalent mutation.
43. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV

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DNA polymerase selected from rtL80V, rtP109S, rtI163V, rtL229M and rtN/H/A/S/Q238K or a combination thereof or an equivalent mutation.

44. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the surface antigen selected from sP120T, sM125F and sT127A or a combination thereof or an equivalent mutation.

45. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the surface antigen selected from sT118R, sM133T, sF134V, sI195M, sS207R and sY225Y/C or a combination thereof or an equivalent mutation.

46. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the surface antigen selected from sS126T, sM133L/M, sS143S/T, sD144A, sG145A and sW172Stop or a combination thereof or an equivalent mutation.

47. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV surface antigen selected from sI81M and sP214Q or a combination thereof or an equivalent mutation.

48. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV surface antigen selected from sF83S, sL173F and sW199L or a combination thereof or an equivalent mutation.

49. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV surface antigen selected from sI126T, sK160R, sS174N, sA184V, sW196L, sS210N, sF/C220L and sY221C or a combination thereof or an equivalent mutation.

50. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV surface antigen selected from sC69Stop/C, sC76Y, sI110V/I, sY134N, sW172Stop/W, sW196Stop and sS207R or a combination thereof or an equivalent mutation.

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51. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtK32, rtN33, rtP34, rtH35 and rtT37 or a combination thereof or an equivalent mutation.
52. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtP59, rtK60, rtF61, rtA62 and rtV63 or a combination thereof or an equivalent mutation.
53. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtD83, rtV84, rtS85, rtA86, rtY89, rtH90 and rtI/L91 or a combination thereof or an equivalent mutation.
54. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtP177, rtF178, rtL179, rtL180, rtA181, rtQ182, rtF183 and rtT184 or a combination thereof or an equivalent mutation.
55. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtM204 and rtY203 or a combination thereof or an equivalent mutation.
56. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rt235, rt236, rt237, rt238 and rt239 or a combination thereof or an equivalent mutation.
57. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rt247, rt248, rt249, rt250 and rt251 or a combination thereof or an equivalent mutation.
58. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from K32M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion; N33D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;

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P34S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
H35I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
T37W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion;
P59S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
K60M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion;
F61P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
A62R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
V63A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion;
D83C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/deletion;
V84A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion;
S85T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/deletion;
A86R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
Y89V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/deletion;
H90I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
I/L91K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/deletion;
P177S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
F178P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
L179K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
L180K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
A181R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
Q183E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/deletion;
F183P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
T184W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion;
Y203V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/deletion;
M204F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/deletion;
L235K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
N236D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
T237W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion;
P237S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
N238D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
H238I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;

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A238R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
 S239T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/deletion;
 Q238E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/deletion;
 K239M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion;
 L247K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
 N248D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
 H248I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
 F249P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
 M250F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/deletion;
 G251H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/deletion; and
 V251A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion.

59. A method for determining the potential for an HBV to exhibit reduced sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV or optionally other nucleoside analogs or other anti-HBV agents, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV DNA polymerase resulting in at least one amino acid substitution, deletion and/or addition in any one or more of domains F and A through E or a region proximal thereto of said DNA polymerase and associated with resistance or decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, wherein the presence of such a mutation is an indication of the likelihood of resistance to said ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV.

60. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to

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ADV.

61. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to LMV.
62. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to TFV.
63. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to FTC.
64. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to ADV and LMV.
65. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to ADV and TFV.
66. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to LMV and TFV.
67. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to ADV and FTC.
68. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to TFV and FTC.
69. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to LMV and FTC.
70. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to ADV and LMV and TFV.
71. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to ADV

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and LMV and FTC.

72. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to LMV and TFV and FTC.

73. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to ADV and FTC and TFV.

74. The method of Claim 59 wherein the HBV exhibits reduced sensitivity to ADV and LMV and TFV and FTC.

75. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtS21A, rtL122F, rtN124H, rtT28N, rtP130Q, rtD131N and rtY135C or a combination thereof or an equivalent mutation.

76. The isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtN/S/T/I/V53D, rtY126Q, rtL180M, rtS202G, rtI204V and rtI235I/M or a combination thereof or an equivalent mutation.

77. The isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtN53D, rtY54H, rtS57P, rtL91I, rtS116P, rtF122L, rtY124H, rtV134D, rtY141Y/F, rtL145M, rtF151F/Y, rtA181T, rtK212R, rtL217R, rtS219A, rtN236T and rtN238D or a combination thereof or an equivalent mutation.

78. The isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtS78T, rtV84M, rtY126C, rtV191I, rtM204I and rtV214A or a combination thereof or an equivalent mutation.

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79. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtH90D and rtL/F108L or a combination thereof or an equivalent mutation.
80. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected rtL157L/M, rtA181V and rtV207I or a combination thereof or an equivalent mutation.
81. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtL80V, rtP109S, rtI163V, rtL229M and rtN/H/A/S/Q238K or a combination thereof or an equivalent mutation.
82. The isolated HBV variant of Claim 1 or 37 comprising a mutation in the DNA polymerase selected from rtS78S/T, rtN118N/S, rtN139N/K, rtV142E, rtA181A/T, rtI204M, rtQ/P/S/Stop215Q, rtE218K/E and rtN238N/H or a combination thereof or an equivalent mutation.
83. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the surface antigen gene selected from sP120T, sM125F and sT127A or a combination thereof or an equivalent mutation.
84. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV Surface antigen gene selected from sT118R, sM133T, sF134V, sI195M, sS207R and sY225Y/C or a combination thereof or an equivalent mutation.
85. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the surface antigen selected from sS126T, sM133L/M, sS143S/T, sD144A, sG145A and sW172Stop or a combination thereof or an equivalent mutation.
86. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA surface antigen selected from sN40S, sC69Stop, sM75I,

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sL88P, sT118A, sW182Stop, sW196L, sY206H and sY225F or a combination thereof or an equivalent mutation.

87. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA surface antigen selected from sI181M and sP214Q or a combination thereof or an equivalent mutation.

88. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA surface antigen selected from sF83S, sL173F and sW199L or a combination thereof or an equivalent mutation.

89. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA surface antigen selected from sI126T, sK160R, sS174N, sA184V, sW196L, sS210N, sF/C220L and sY221C or a combination thereof or an equivalent mutation.

90. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA surface antigen selected from sC69Stop/C, sC76Y, sI110V/I, sY134N, sW172Stop/W, sW196Stop and sS207R or a combination thereof or an equivalent mutation.

91. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtK32, rtN33, rtP34, rtH35 and rtT37 or a combination thereof or an equivalent mutation.

92. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtP59, rtK60, rtF61, rtA62 and rtV63 or a combination thereof or an equivalent mutation.

93. An isolated DNA molecule from an HBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtD83, rtV84, rtS85, rtA86, rtY89,

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rtH90 and rtI/L91 or a combination thereof or an equivalent mutation.

94. An isolated DNA molecule from anHBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtP177, rtF178, rtL179, rtL180, rtA181, rtQ182, rtF183 and rtT184 or a combination thereof or an equivalent mutation.

95. An isolated DNA molecule from anHBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rtM204 and rtY203 or a combination thereof or an equivalent mutation.

96. An isolated DNA molecule from anHBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rt235, rt236, rt237, rt238 and rt239 or a combinations thereof or an equivalent mutation.

97. An isolated DNA molecule from anHBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerase selected from rt247, rt248, rt249, rt250 and rt251 or a combinations thereof or an equivalent mutation.

98. An isolated DNA molecule from anHBV variant of Claim 1 or 37 comprising a mutation in the HBV DNA polymerases selected from K32M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion; N33D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion; P34S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion; H35I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion; T37W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion; P59S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion; K60M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion; F61P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion; A62R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion; V63A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion; D83C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/deletion;

V84A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion;
S85T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/deletion;
A86R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/YV/deletion;
Y89V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/deletion;
H90I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
I/L91K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/deletion;
P177S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
F178P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
L179K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
L180K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
A181R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
Q183E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/deletion;
F183P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
T184W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion;
Y203V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/deletion;
M204F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/deletion;
L235K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
N236D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
T237W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion;
P237S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
N238D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
H238I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
A238R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
S239T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/deletion;
Q238E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/deletion;
K239M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion;
L247K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
N248D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
H248I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
F249P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
M250F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/deletion;

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G251H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/deletion; and
V251A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion.

99. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rtS21A, rtL122F, rtN124H, rtT28N, rtP130Q, rtD131N and rtY135C or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

100. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rtN/S/T/I/V53D, rtY126Q, rtL180M, rtS202G, rtI204V and rtI235I/M or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

101. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rtN53D, rtY54H, rtS57P, rtL91I, rtS116P, rtF122L, rtY124H, rtV134D, rtY141Y/F, rtL145M, rtF151F/Y, rtA181T, rtK212R, rtL217R, rtS219A, rtN236T and rtN238D or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and

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LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

102. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rtS78T, rtV84M, rtY126C, rtV191I, rtM204I and rtV214A or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV and optionally other nucleoside analogs.

103. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rtH90D and rtL/F108L or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

104. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rtL157L/M, rtA181V and rtV207I or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and

optionally other nucleoside analogs.

105. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rtL80V, rtP109S, rtI163V, rtL229M and rtN/H/A/S/Q238K or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

106. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rtS78S/T, rtN118N/S, rtN139N/K, rtV142E, rtA181A/T, rtI204M, rtQ/P/S/Stop215Q, rtE218K/E and rtN238N/H or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

107. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of sP120T, sM125F and sT127A or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally

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other nucleoside analogs.

108. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of sT118R, sM133T, sF134V, sI195M, sS207R and sY225Y/C or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.
109. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of sS126T, sM133L/M, sS143S/T, sD144A, sG145A and sW172Stop or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.
110. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of sN40S, sC69Stop, sM75L, sL88P, sT118A, sW182Stop, sW196L, sY206H and sY225F or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

111. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of s181M and sP214Q or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

112. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of sF83S, sL173F and sW199L or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

113. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of sI126T, sK160R, sS174N, sA184V, sW196L, sS210N, sF/C220L and sY221C or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

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114. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of sC69Stop/C, sC76Y, sI110V/I, sY134N, sW172Stop/W, sW196Stop and sS207R or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.
115. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rtK32, rtN33, rtP34, rtH35 and rtT37 or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.
116. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rtP59, rtK60, rtF61, rtA62 and rtV63 or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.
117. A method for determining whether an HBV strain exhibits reduced sensitivity

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to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rtD83, rtV84, rtS85, rtA86, rtY89, rtH90 and rtI/L91 or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

118. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rtP177, rtF178, rtL179, rtL180, rtA181, rtQ182, rtF183 and rtT184 or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

119. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rtM204 and rtY203 or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

120. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA

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from said HBV and screening for a mutation wherein the presence of rt235, rt236, rt237, rt238 and rt239 or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

121. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of rt247, rt248, rt249, rt250 and rt251 or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside analogs.

122. A method for determining whether an HBV strain exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation wherein the presence of K32M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion;
N33D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
P34S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
H35I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
T37W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion;
P59S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
K60M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion;
F61P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
A62R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
V63A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion;

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D83C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/deletion;
V84A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion;
S85T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/deletion;
A86R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/YV/deletion;
Y89V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/deletion;
H90I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
I/L91K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/deletion;
P177S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
F178P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
L179K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
L180K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
A181R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/YV/deletion;
Q183E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/deletion;
F183P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
T184W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion;
Y203V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/deletion;
M204F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/deletion;
L235K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
N236D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
T237W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion;
P237S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
N238D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
H238I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
A238R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
S239T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/deletion;
Q238E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/deletion;
K239M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion;
L247K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
N248D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
H248I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
F249P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;

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M250F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/deletion;
G251H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/deletion; and
V251A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV and optionally other nucleoside analogs.

123. A method for detecting an agent which exhibits inhibitory activity to an HBV which exhibits resistance or decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV and optionally other nucleoside or nucleotide analogs or other anti-HBV agents, said method comprising:

generating a genetic construct comprising a replication competent-effective amount of the genome from said HBV contained in a plasmid vector and then transfecting said cells with said construct;

contacting said cells, before, during and/or after transfection, with the agent to be tested;

culturing said cells for a time and under conditions sufficient for the HBV to replicate, express genetic sequences and/or assemble and/or release virus or virus-like particles if resistant to said agent; and

subjecting the cells, cell lysates or culture supernatant fluid to viral- or viral-component-detection means to determine whether or not the virus has replicated, expressed genetic material and/or assembled and/or been released in the presence of said agent.

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124. A method for detecting an agent which exhibits inhibitory activity to an HBV which exhibits resistance or decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV, and optionally other nucleoside or nucleotide analogs or other anti-HBV agents, said method comprising:

generating a genetic construct comprising a replication competent-effective amount of the genome from said HBV contained in or fused to an amount of a baculovirus genome effective to infect cells and then infecting said cells with said construct;

contacting said cells, before, during and/or after infection, with the agent to be tested;

culturing said cells for a time and under conditions sufficient for the HBV to replicate, express genetic sequences and/or assemble and/or release virus or virus-like particles if resistant to said agent; and

subjecting the cells, cell lysates or culture supernatant fluid to viral- or viral-component-detection means to determine whether or not the virus has replicated, expressed genetic material and/or assembled and/or been released in the presence of said agent.

125. The method of Claim 123 or 124 wherein the HBV genome is stably integrated into the cells' genome.

126. An agent identified by the method of any one of Claims 123 to 124.

127. Use of an HBV variant according to any one of Claims 1 to 59 or a component thereof in the rational design of an anti-HBV agent.

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128. Use according to Claim 126 wherein the rational design comprises microarray analysis.
129. Use according to Claim 126 wherein the rational design is based on the crystal structure or NMR structure of a viral component.
130. A vaccine comprising an antigenic component of the HBV variant of any one of Claims 1 to 59 or an antigenic component thereof or an antibody thereto.
131. The vaccine of Claim 130 wherein the antigenic component is an HBsAg or PreS1 or PreS2.
132. The vaccine of Claim 130 wherein the antigenic component is a defective HBV variant.
133. The vaccine of Claim 130 comprising an antibody to HBsAg or PreS1 or PreS2
134. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rtS21A, rtL122F, rtN124H, rtT28N, rtP130Q, rtD131N and rtY135C.
135. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rtN/S/T/I/V53D, rtY126Q, rtL180M, rtS202G, rtI204V and rtI235I/M.
136. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rtN53D, rtY54H, rtS57P, rtL91I, rtS116P, rtF122L, rtY124H, rtV134D, rtY141Y/F. --

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137. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rtL145M, rtF151F/Y, rtA181T, rtK212R, rtL217R, rtS219A, rtN236T and rtN238D.

138. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rtS78T, rtV84M, rtY126C, rtV191I, rtM204I and rtV214A.

139. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rtH90D and rtL/F108L.

140. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rtL157L/M, rtA181V and rtV207I.

141. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rtL80V, rtP109S, rtI163V, rtL229M and rtN/H/A/S/Q238K.

142. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rtS78S/T, rtN118N/S, rtN139N/K, rtV142E, rtA181A/T, rtI204M, rtQ/P/S/Stop215Q, rtE218K/E and rtN238N/H.

143. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from sP120T, sM125F and sT127A.

144. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from sT118R, sM133T, sF134V, sI195M, sS207R and sY225Y/C.

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145. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from sS126T, sM133L/M, sS143S/T, sD144A, sG145A and sW172Stop.
146. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from sN40S, sC69Stop, sM75I, sL88P, sT118A, sW182Stop, sW196L, sY206H and sY225F.
147. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from sI81M and sP214Q.
148. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from sF83S, sL173F and sW199L.
149. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from sI126T, sK160R, sS174N, sA184V, sW196L, sS210N, sF/C220L and sY221C.
150. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from sC69Stop/C, sC76Y, sI110V/I, sY134N, sW172Stop/W, sW196Stop and sS207R.
151. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rK32, rN33, rP34, rH35 and rT37.
152. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rP59, rK60, rF61, rA62 and rV63.
153. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rD83, rV84, rS85, rA86, rY89, rH90 and rI/L91.

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154. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rtP177, rtF178, rtL179, rtL180, rtA181, rtQ182, rtF183 and rtT184.

155. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rtM204 and rtY203.

156. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rt235, rt236, rt237, rt238 and rt239.

157. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from rt247, rt248, rt249, rt250 and rt251.

158. The vaccine of Claim 130 wherein the HBV or its antigenic compound is from an HBV variant having a mutation selected from,
 K32M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion;
 N33D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
 P34S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
 H35I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
 T37W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion;
 P59S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
 K60M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion;
 F61P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
 A62R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
 V63A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion;
 D83C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/deletion;
 V84A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion;
 S85T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/deletion;
 A86R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
 Y89V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/deletion;

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H90I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
I/L91K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/deletion;
P177S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
F178P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
L179K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
L180K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
A181R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
Q183E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/deletion;
F183P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
T184W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion;
Y203V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/deletion;
M204F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/deletion;
L235K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
N236D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
T237W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion;
P237S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
N238D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
H238I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
A238R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
S239T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/deletion;
Q238E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/deletion;
K239M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion;
L247K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
N248D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
H248I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
F249P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
M250F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/deletion;
G251H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/deletion; and
V251A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion.

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159. A computer product for assessing the likely usefulness of a viral variant or biological sample comprising same for determining an appropriate therapeutic protocol in a subject, said product comprising:

- (1) code that receives as input index values (I_{vs}) for at least two features associated with said viral agents or biological sample comprising same, wherein said features are selected from:
 - (a) the ability to exhibit resistance for reduced sensitivity to a particular compound or immunological agent;
 - (b) an altered DNA polymerase from wild-type HBV;
 - (c) an altered surface antigen from wild-type HBV;
 - (d) morbidity or recovery potential of a patient; or
 - (e) altered replication capacity (increased or decreased);
- (2) code that adds said I_{vs} to provide a sum corresponding to a potency value (P_v) for said viral variants or biological samples; and
- (3) a computer readable medium that stores the codes.

160. A computer for assessing the likely usefulness of a viral variant or biological sample comprising same in a subject, wherein said computer comprises:

- (1) a machine-readable data storage medium comprising a data storage material encoded with machine-readable data, wherein said machine-readable data comprise I_{vs} for at least two features associated with said viral variant or biological sample; wherein said features are selected from:-
 - (a) the ability to exhibit resistance for reduced sensitivity to a particular compound or immunological agent;

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- (b) an altered DNA polymerase from wild-type HBV;
 - (c) an altered surface antigen from wild-type HBV;
 - (d) morbidity or recovery potential of a patient; or
 - (e) altered replication capacity (increased or decreased);
- (2) a working memory for storing instructions for processing said machine-readable data;
 - (3) a central-processing unit coupled to said working memory and to said machine-readable data storage medium, for processing said machine readable data to provide a sum of said I_{vs} corresponding to a P_v for said compound(s); and
 - (4) an output hardware coupled to said central processing unit, for receiving said P_v .

161. A composition comprising an agent capable of directly or indirectly inhibiting an HBV variant as defined in any one of Claims 1 to 59, said composition further comprising one or more pharmaceutically acceptable carriers and/or diluents.

162. The composition of Claim 161 wherein the agent is a recombinant protein from said HBV variant.

163. The composition of Claim 161 wherein the recombinant protein is HBsAg or PreS1 or PreS2.

164. The composition of Claim 161 wherein the agent is capable of inhibiting an HBV variant polymerase.

165. The composition of Claim 161 wherein the agent is identified by natural product screening or rational drug design.

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166. The composition of Claim 161 wherein the agent is a defective HBV variant.

167. The composition of Claim 161 wherein the agent is an antibody directed to an HBV compound.

168. The composition of Claim 161 wherein the agent is a ribozyme, antisense molecule or sense molecule relative to an HBV gene.

169. A method according to Claims 37 to 57 wherein a virus related to HBV from the family of hepadnaviruses such as WHV or DHBV exhibits reduced sensitivity to a nucleoside analog, said method comprising isolating DNA or corresponding mRNA from said HBV, or DHBV or WHV and screening for a mutation or combinations thereof or an equivalent one or more other mutation is indicative of a variant wherein said variant exhibits a decreased sensitivity to ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV.

170. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

171. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA

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or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from sP120T, sM125T and sT127A selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

172. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from sT118R, sM133T, sF134V sI195M, sS207R and sY225Y/C selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

173. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from sS126T, sM133L/M, sS143S/T, sD144A sG145A and sW172Stop selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

174. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from sN40S, and sC69 Stop, sM75I, sL88P, sT118A, sW182stop, sW196L, sY206H and sY225F selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

175. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from sF83S, sL173F and sW199L selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

176. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from sI126T, sK160R, sS174N, sA184V, sW196L, sS210N, sF/C220L and sY221C selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and

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LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

177. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from sC69Stop/C, sC76Y sI110V/I, sY134N, sW172Stop/W, sW196Stop and sS207R selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

178. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

179. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rtS21A, rtL122F, rtN124H, rtH126R,

rtT128N, rtP130Q, rtD131N, rtY135C selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

180. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rtN/S/T/I/V53D, rtY126Q, rtL180M, rtS202G, rtI204V, rtI235I/M selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

181. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rtN53D, rtY54H, rtS57P, rtL91I, rtS116P, rtF122L, rtY124H, rtV134D, rtY141Y/F, rtL145M, rtF151F/Y, rtA181T, rtK212R, rtL217R, rtS219A, rtN236T and rtN238D selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

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182. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rtS78T, rtV84M, rtY126C, rtV191L, rtM204I and rtV214A selected during treatment with ADV, LMV, TFFV, or FTC, or ADV and LMV, ADV and TFFV, LMV and TFFV, FTC and ADV, FTC and TFFV, FTC and LMV, or ADV and LMV and TFFV, or ADV and FTC and TFFV, TFFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.
183. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rtH90D and rtL/F108L selected during treatment with ADV, LMV, TFFV, or FTC, or ADV and LMV, ADV and TFFV, LMV and TFFV, FTC and ADV, FTC and TFFV, FTC and LMV, or ADV and LMV and TFFV, or ADV and FTC and TFFV, TFFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.
184. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rtL157L/M, rtA181V, rtV207I; and rtN236T selected during treatment with ADV, LMV, TFFV, or FTC, or ADV and LMV, ADV and TFFV, LMV and TFFV, FTC and ADV, FTC and TFFV, FTC and LMV, or ADV and LMV and TFFV, or ADV and FTC and TFFV, TFFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFFV is an indication of the likelihood of reducing

interactivity of said antibodies to said mutated surface antigen.

185. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rtL80V, rtP109S, rtI163V, rtM204I, rtL229M and rtN/H/A/S/Q238K selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

186. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rtS78S/T, rtN118N/S, rtN139N/K, rtV142E, rtA181A/T, rtI204M, rtQ/P/S/Stop215Q, rtE218K/E, and rtN238N/H selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

187. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rtK32, rtN33, rtP34, rtH35 and rtT37 selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV,

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LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

188. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rtP59, rtK60, rtF61, rtA62 and rtV63 elected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

189. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rtD83, rtV84, rtS85, rtA86, rtY89, rtH90 selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

190. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the

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presence of such a mutation is selected from rtP177, rtF178, rtL179, rtL180, rtA181, rtQ182, rtF183 and rtT184 selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

191. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rtM204 and rtY203 selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

192. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rt235, rt236, rt237, rt238 and rt239 selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

193. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA

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or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation is selected from rt247, rt248, rt249, rt250 and rt251 selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

194. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolating DNA or corresponding mRNA from said HBV and screening for a mutation in the nucleotide sequence encoding HBV surface antigen and/or HBV DNA polymerase genes wherein the presence of such a mutation, K32M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion; N33D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion; P34S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion; H35I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion; T37W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion; P59S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion; K60M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion; F61P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion; A62R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion; V63A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion; D83C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/deletion; V84A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion; S85T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/deletion; A86R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion; Y89V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/deletion; H90I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion; I/L91K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/deletion; P177S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;

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F178P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
 L179K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
 L180K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
 A181R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
 Q183E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/deletion;
 F183P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
 T184W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion;
 Y203V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/deletion;
 M204F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/deletion;
 L235K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
 N236D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
 T237W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/deletion;
 P237S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/deletion;
 N238D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
 H238I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
 A238R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/deletion;
 S239T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/deletion;
 Q238E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/deletion;
 K239M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/deletion;
 L247K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/deletion;
 N248D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/V/A/R/deletion;
 H248I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/deletion;
 F249P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/M/deletion;
 M250F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/G/H/I/L/K/deletion;
 G251H/I/L/K/M/F/P/S/T/W/Y/V/A/R/N/D/C/Q/E/deletion; and
 V251A/R/N/D/C/Q/E/G/H/I/L/K/M/F/P/S/T/W/Y/deletion, is selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

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195. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolated protein from said HBV encoding HBV surface antigen wherein the presence of such a mutation was selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV and is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.
196. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolated protein from said HBV encoding HBV surface antigen wherein the presence of such a mutation is selected from sP120T, sM125T and sT127A selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.
197. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolated protein from said HBV encoding HBV surface antigen wherein the presence of such a mutation was selected from sT118R, sM133T, sF134V sI195M, sS207R and sY225Y/C selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

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198. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolated protein from said HBV encoding HBV surface antigen wherein the presence of such a mutation was selected from sS126T, sM133L/M, sS143S/T, sD144A sG145A and sW172Stop selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

199. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolated protein from said HBV encoding HBV surface antigen wherein the presence of such a mutation was selected from sN40S, and sC69 Stop, sM75I, sL88P, sT118A, sW182stop, sW196L, sY206H and sY225F selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

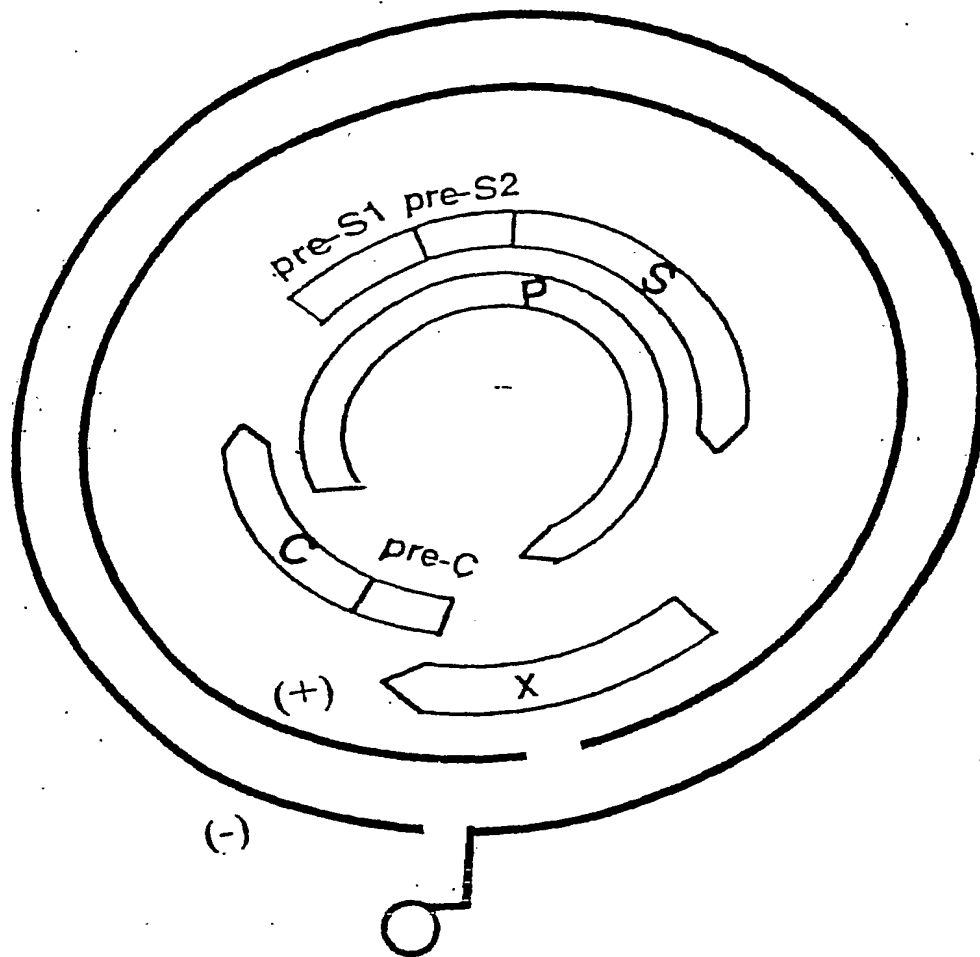
200. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolated protein from said HBV encoding HBV surface antigen wherein the presence of such a mutation was selected from sF83S, sL173F and sW199L selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen

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201. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolated protein from said HBV encoding HBV surface antigen wherein the presence of such a mutation was selected from sI126T, sK160R, sS174N, sA184V, sW196L, sS210N, sF/C220L and sY221C selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

202. A method for determining the potential for an HBV to exhibit reduced interactivity to antibody to HBV surface antigen, said method comprising isolated protein from said HBV encoding HBV surface antigen wherein the presence of such a mutation was selected sC69Stop/C, sC76Y sI110V/I, sY134N, sW172Stop/W, sW196Stop and sS207R selected during treatment with ADV, LMV, TFV, or FTC, or ADV and LMV, ADV and TFV, LMV and TFV, FTC and ADV, FTC and TFV, FTC and LMV, or ADV and LMV and TFV, or ADV and FTC and TFV, TFV and FTC and LMV, ADV and LMV and FTC, or ADV and FTC and LMV and TFV is an indication of the likelihood of reducing interactivity of said antibodies to said mutated surface antigen.

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**Figure 1**

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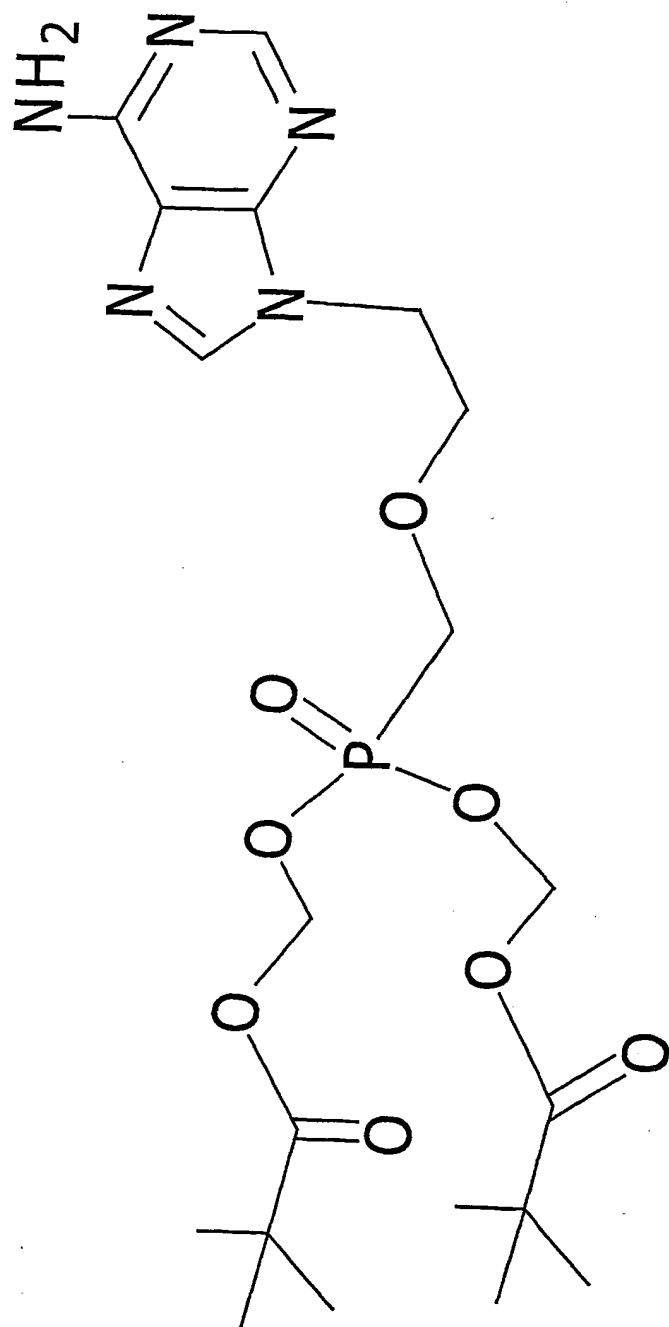
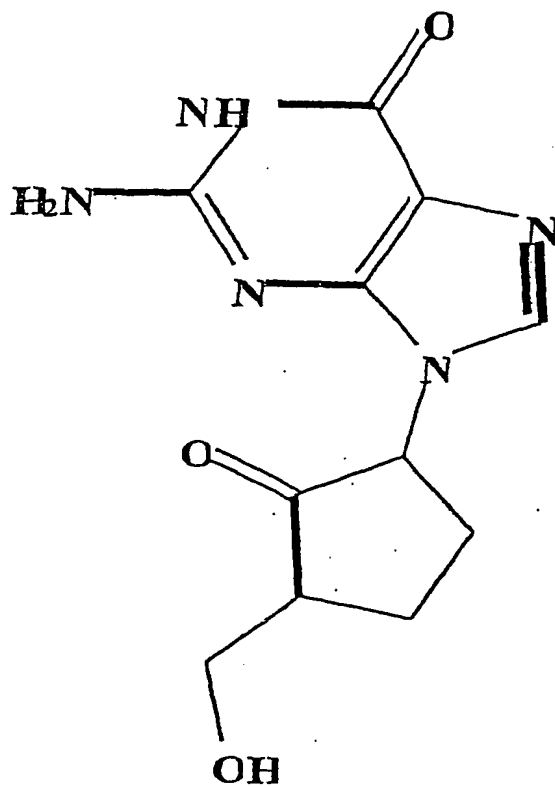


Figure 2

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**Figure 3**

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IL1A1 F, A-E	1	CAAACTTGGCAGCAATCCGGCTCTCTCCATVACCAATCGCCAGTCAGGAGGAGCCTACCCCGCTGTCTCCACCTTT	80	[SEQ ID NO:8]
IL1A 2 F, A-E	1	GCAATCTACAAA-CTTTGGCAGCAATCCGGCTCTCTCCATVACCAATCGCCAGTCAGGAGGAGCCTACCCCGCTGTCTCCACCTTT	88	[SEQ ID NO:9]
IL1A 3 F, A-E	1	ACTAGCTCAGGCAATCTACAAAATTTGGCAGCAATCCGGCTCTCTCCATVACCAATCGCCAGTCAGGAGGAGCCTACCCCGCTGTCTCCACCTTT	100	[SEQ ID NO:10]
IL1A 4 F, A-E	1	TGCCAGCAATCCGGCTCTCTCCATVACCAATCGCCAGTCAGGAGGAGCCTACCCCGCTGTCTCCACCTTT	73	[SEQ ID NO:11]
IL1A1 F, A-E	81	GAGAAACACTCATCTCAGGCCATGAGTGAATTCACAACTTCCACCACTCTGAAAGATCCAGAGTGARAGGCCCTGTATTTCCCTGCTGGTGGC	173	
IL1A 2 F, A-E	89	GAGAAACACTCATCTCAGGCCATGAGTGAATTCACAACTTCCACCACTCTGAAAGATCCAGAGTGARAGGCCCTGTATTTCCCTGCTGGTGGC	180	
IL1A 3 F, A-E	101	GAGAAACACTCATCTCAGGCCATGAGTGAATTCACAACTTCCACCACTCTGAAAGATCCAGAGTGARAGGCCCTGTATTTCCCTGCTGGTGGC	188	
IL1A 4 F, A-E	74	GAGAAACACTCATCTCAGGCCATGAGTGAATTCACAACTTCCACCACTCTGAAAGATCCAGAGTGARAGGCCCTGTATTTCCCTGCTGGTGGC	200	
IL1A1 F, A-E	181	TCCAGTTTCAGGAAACAGTAAACCCCTGTTCCGACTACTGCTCTCCATATCTGTAATCTTCTCGAGGATTTGGGACCCCTGCGCTGAACATGAGAAACATCA	273	
IL1A 2 F, A-E	189	TCCAGTTTCAGGAAACAGTAAACCCCTGTTCCGACTACTGCTCTCCATATCTGTAATCTTCTCGAGGATTTGGGACCCCTGCGCTGAACATGAGAAACATCA	280	
IL1A 3 F, A-E	201	TCCAGTTTCAGGAAACAGTAAACCCCTGTTCCGACTACTGCTCTCCATATCTGTAATCTTCTCGAGGATTTGGGACCCCTGCGCTGAACATGAGAAACATCA	288	
IL1A 4 F, A-E	174	TCCAGTTTCAGGAAACAGTAAACCCCTGTTCCGACTACTGCTCTCCATATCTGTAATCTTCTCGAGGATTTGGGACCCCTGCGCTGAACATGAGAAACATCA	300	
IL1A1 F, A-E	281	CATCAGGATTTCTMGAGCCCTKCTCGTGTACAGCGGGGTTTTTCTGTTGACAGAAATCTTCAATACCGCAGAGTCTAGACTCGTGGTGGACTTC	373	
IL1A 2 F, A-E	289	CATCAGGATTTCTMGAGCCCTKCTCGTGTACAGCGGGGTTTTTCTGTTGACAGAAATCTTCAATACCGCAGAGTCTAGACTCGTGGTGGACTTC	380	
IL1A 3 F, A-E	301	CATCAGGATTTCTMGAGCCCTKCTCGTGTACAGCGGGGTTTTTCTGTTGACAGAAATCTTCAATACCGCAGAGTCTAGACTCGTGGTGGACTTC	388	
IL1A 4 F, A-E	274	CATCAGGATTTCTMGAGCCCTKCTCGTGTACAGCGGGGTTTTTCTGTTGACAGAAATCTTCAATACCGCAGAGTCTAGACTCGTGGTGGACTTC	400	
IL1A1 F, A-E	381	TCTCAATTTTCTAGGGGAACTACCGTGTGTTTTCAGGCGGGGTTTTTCTGTTGACAGAAATCTTCAATACCGCAGAGTCTAGACTCGTGGTGGACTTC	473	
IL1A 2 F, A-E	389	TCTCAATTTTCTAGGGGAACTACCGTGTGTTTTCAGGCGGGGTTTTTCTGTTGACAGAAATCTTCAATACCGCAGAGTCTAGACTCGTGGTGGACTTC	480	
IL1A 3 F, A-E	401	TCTCAATTTTCTAGGGGAACTACCGTGTGTTTTCAGGCGGGGTTTTTCTGTTGACAGAAATCTTCAATACCGCAGAGTCTAGACTCGTGGTGGACTTC	488	
IL1A 4 F, A-E	374	TCTCAATTTTCTAGGGGAACTACCGTGTGTTTTCAGGCGGGGTTTTTCTGTTGACAGAAATCTTCAATACCGCAGAGTCTAGACTCGTGGTGGACTTC	500	
IL1A1 F, A-E	481	TATCGCTGGATGTCTGCGGGTTTTTATCATCTTCTCTGCTGCTATGCTCATCTTCTGTTGTTTCTTCTGGACTATCAAGGTATGTTGC	573	
IL1A 2 F, A-E	489	TATCGCTGGATGTCTGCGGGTTTTTATCATCTTCTCTGCTGCTATGCTCATCTTCTGTTGTTTCTTCTGGACTATCAAGGTATGTTGC	580	
IL1A 3 F, A-E	501	TATCGCTGGATGTCTGCGGGTTTTTATCATCTTCTCTGCTGCTATGCTCATCTTCTGTTGTTTCTTCTGGACTATCAAGGTATGTTGC	588	
IL1A 4 F, A-E	474	TATCGCTGGATGTCTGCGGGTTTTTATCATCTTCTCTGCTGCTATGCTCATCTTCTGTTGTTTCTTCTGGACTATCAAGGTATGTTGC	600	
IL1A1 F, A-E	581	CCGTTTGTCTTAATTCAGGATCTTCAACCAACGCGGGGAMCATGAGAACCTGACAGACTCTGCTCAAGGAACTCTATGATATCCCTCTCTGTTG	673	
IL1A 2 F, A-E	589	CCGTTTGTCTTAATTCAGGATCTTCAACCAACGCGGGGAMCATGAGAACCTGACAGACTCTGCTCAAGGAACTCTATGATATCCCTCTCTGTTG	680	
IL1A 3 F, A-E	601	CCGTTTGTCTTAATTCAGGATCTTCAACCAACGCGGGGAMCATGAGAACCTGACAGACTCTGCTCAAGGAACTCTATGATATCCCTCTCTGTTG	688	
IL1A 4 F, A-E	574	CCGTTTGTCTTAATTCAGGATCTTCAACCAACGCGGGGAMCATGAGAACCTGACAGACTCTGCTCAAGGAACTCTATGATATCCCTCTCTGTTG	700	
IL1A1 F, A-E	681	CTGTACCAACCTTCGGACGGAAACTGCACTGTATTTCCATCCCATCTCTGGGCTTTTCGGAAATTCCTATGGGAGTGGGCCCTCAGCCCGTTTCTCC	773	
IL1A 2 F, A-E	689	CTGTACCAACCTTCGGACGGAAACTGCACTGTATTTCCATCCCATCTCTGGGCTTTTCGGAAATTCCTATGGGAGTGGGCCCTCAGCCCGTTTCTCC	780	
IL1A 3 F, A-E	701	CTGTACCAACCTTCGGACGGAAACTGCACTGTATTTCCATCCCATCTCTGGGCTTTTCGGAAATTCCTATGGGAGTGGGCCCTCAGCCCGTTTCTCC	788	
IL1A 4 F, A-E	674	CTGTACCAACCTTCGGACGGAAACTGCACTGTATTTCCATCCCATCTCTGGGCTTTTCGGAAATTCCTATGGGAGTGGGCCCTCAGCCCGTTTCTCC	800	

Figure 4

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IL1A1 F, A-E	781	TGGCTCAGTTTACTAGTGCCATTGTTTCAGTGGTTCTAGGGCTTTCCCCCACTGTTGGCTTTCAGTTATATGGATGATGGTATTGGGGCCCAAGTC	880	[SEQ ID NO:8]
IL1A 2 F, A-E	789	TGGCTCAGTTTACTAGTGCCATTGTTTCAGTGGTTCTAGGGCTTTCCCCCACTGTTGGCTTTCAGTTATATGGATGATGGTATTGGGGCCCAAGTC	888	[SEQ ID NO:9]
IL1A 3 F, A-E	801	TGGCTCAGTTTACTAGTGCCATTGTTTCAGTGGTTCTAGGGCTTTCCCCCACTGTTGGCTTTCAGTTATATGGATGATGGTATTGGGGCCCAAGTC	900	[SEQ ID NO:10]
IL1A 4 F, A-E	774	TGGCTCAGTTTACTAGTGCCATTGTTTCAGTGGTTCTAGGGCTTTCCCCCACTGTTGGCTTTCAGTTATATGGATGATGGTATTGGGGCCCAAGTC	873	[SEQ ID NO:11]
IL1A1 F, A-E	881	TGTAYAGCAVCTTGAGTCCCTTTTACCGCTCTTACCAATTTCTTTGCTTTGGGTATACATTTAAACCCCTAAACAACCTAAAGATGGGGTTACTCT	980	
IL1A 2 F, A-E	889	TGTACAGCATCTTGAGTCCCTTTTACCGCTCTTACCAATTTCTTTGCTTTGGGTATACATTTAAACCCCTAAACAACCTAAAGATGGGGTTACTCT	988	
IL1A 3 F, A-E	901	TGTACAGCATCTTGAGTCCCTTTTACCGCTCTTACCAATTTCTTTGCTTTGGGTATACATTTAAACCCCTAAACAACCTAAAGATGGGGTTACTCT	1000	
IL1A 4 F, A-E	874	TGTACAGCATCTTGAGTCCCTTTTACCGCTCTTACCAATTTCTTTGCTTTGGGTATACATTTAAACCCCTAAACAACCTAAAGATGGGGTTACTCT	973	
IL1A1 F, A-E	981	TTACATTTTCATGGGNTATGTCATGGATGTTATGGTCAATTGGCCCAAGATCACATCATACAGAAAAATCAAGATGGTTT	1060	
IL1A 2 F, A-E	989	CTAAATTTTATGGGTTATGTCATTTGGATGTTATGGTCTCTTG	1030	
IL1A 3 F, A-E	1001	CTAAATTTTATGGGTTATGTCATTTGGATGTTATGGTCTCTTGCCACAAGAACACATCATACAAAAAAATCAAGAAATG	1077	
IL1A 4 F, A-E	974	TTAAATTTTCATGGGNTATGTCATTTGGATGTTATGGG	1010	

Figure 4 (continued)

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Patient A polymerase amino acid sequence alignment

Pol Trans Pre 1	KLASKASSIXQSPVRXAAYPVSTFEKHSSSGHAEVXHNLPNSRXRSQXERPVFPQWMLQFRNSKPCSDYCLSHIVNLLDWDGPCAHEGHH	93	[SEQ ID NO:12]
Pol Trans 2	HTTNFASKGASCLHQSPVRKAAYPVSTFEKHSSSGHAEVFNHLPNSARSQSERPVFPQWMLQFRNSKPCSDYCLSHIVNLLDWDGPCAHEGHH	96	[SEQ ID NO:13]
Pol Trans 3	LAQGILQNFASKGASCLHQSPVRKAAYPVSTFEKHSSSGHAEVFNHLPNSARSQSERPVFPQWMLQFRNSKPCSDYCLSHIVNLLDWDGPCAHEGHH	100	[SEQ ID NO:14]
Pol Trans 4	ASKGASSIYQSPVGTAAYPVSTFEKHSSSGHAEVFNHLPNSARSQSERPVFPQWMLQFRNSKPCSDYCLSHIVNLLDWDGPCAHEGHH	91	[SEQ ID NO:15]
Pol Trans Pre 94	IRIPRTPXRVGTGGVFLVDKPNHNTAESRLVVDFFSQFSGRGNYRVSWPKFAVFNLSLSSNLSLSDVSAAFYHLPHPAAMPHLLVSGSGLSRYVA	193	
Pol Trans 2 97	IRIPRTPSRVTGGVFLVDKPNHNTAESRLVVDFFSQFSGRGNYRVSWPKFAVFNLSLSSNLSLSDVSAAFYHLPHPAAMPHLLVSGSGLSRYVA	196	
Pol Trans 3 101	IRIPRTPSRVTGGVFLVDKPNHNTAESRLVVDFFSQFSGRGNYRVSWPKFAVFNLSLSSNLSLSDVSAAFYHLPHPAAMPHLLVSGSGLSRYVA	200	
Pol Trans of 4 92	IRIPRTPARVTGGVFLVDKPNHNTAESRLVVDFFSQFSGRGNYRVSWPKFAVFNLSLSSNLSLSDVSAAFYHLPHPAAMPHLLVSGSGLSRYVA	191	
Pol Trans Pre 194	RLSSNSRIFNHQRGMQNLHDYCSRNLYVSLLLLYQTFFGRKLHLYSHPIILGFRKIPMGVGLSPFLAQFTSAICSVVRRAFPCHLAFSYMDVVLGAKS	293	
Pol Trans 2 197	RLSSNSRIILNNQHGTMVDLHDYCSRNLYVSLLLLYQTFFGRKLHLYSHPIILGFRKIPMGVGLSPFLAQFTSAICSVVRRAFPCHLAFSYMDVVLGAKS	296	
Pol Trans 3 201	RLSSNSRIILNNQHGTMVDLHDYCSRNLYVSLLLLYQTFFGRKLHLYSHPIILGFRKIPMGVGLSPFLAQFTSAICSVVRRAFPCHLAFSYMDVVLGAKS	300	
Pol Trans 4 192	RLSSNSRIFNHQRGMQNLHDYCSRNLYVSLLLLYQTFFGRKLHLYSHPIILGFRKIPMGVGLSPFLAQFTSAICSVVRRAFPCHLAFSYMDVVLGAKS	291	
Pol Trans Pre 294	VXHLESIFTAVTNFLLSLGIHNPKNKTRWGYSINFMGVYIGC	336	
Pol Trans 2 297	VQHLESIFTAVTNFLLSLGIHNPKNKTRWGYSINFMGVYIGC	340	
Pol Trans 3 301	VQHLESIFTAVTNFLLSLGIHNPKNKTRWGYSINFMGVYIGC	344	
Pol Trans 4 292	VQHLESIFTAVTNFLLSLGIHNPKNKTRWGYSINFMGVYIGC	336	

Figure 5

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Patient A HBsAg Amino acid alignment

HBsAg Trans of	Pre	1	PPASTNRQSGRQPTPLSPPLRNTHTPQAMQWNSSTTHQTLQDPRVRGLYFPAGSSSGTVNPLVTTASPLSSIFSRIGDPPALNMENITSGFLGPLLVLQA	17	MENITSGFLGPLLVLQA
HBsAg Trans of	2	1	PPASTNRQSGRQPTPLSPPLRNTHTPQAMQWNSSTTHQTLQDPRVRGLYFPAGSSSGTVNPLVTTASPLSSIFSRIGDPPALNMENITSGFLGPLLVLQA	100	PPASTNRQSGRQPTPLSPPLRNTHTPQAMQWNSSTTHQTLQDPRVRGLYFPAGSSSGTVNPLVTTASPLSSIFSRIGDPPALNMENITSGFLGPLLVLQA
HBsAg Trans of	3	1	PPASTNRQSGRQPTPLSPPLRNTHTPQAMQWNSSTTHQTLQDPRVRGLYFPAGSSSGTVNPLVTTASPLSSIFSRIGDPPALNMENITSGFLGPLLVLQA	100	PPASTNRQSGRQPTPLSPPLRNTHTPQAMQWNSSTTHQTLQDPRVRGLYFPAGSSSGTVNPLVTTASPLSSIFSRIGDPPALNMENITSGFLGPLLVLQA
HBsAg Trans of	4	1	PPASTNRQSGRQPTPLSPPLRNTHTPQAMQWNSSTTHQTLQDPRVRGLYFPAGSSSGTVNPLVTTASPLSSIFSRIGDPPALNMENITSGFLGPLLVLQA	100	PPASTNRQSGRQPTPLSPPLRNTHTPQAMQWNSSTTHQTLQDPRVRGLYFPAGSSSGTVNPLVTTASPLSSIFSRIGDPPALNMENITSGFLGPLLVLQA
HBsAg Trans of	Pre	18	GFLLTRILTIPOSLSWNTSINFLGGTTVCLGQNSQSPTSNHSPTSCPPTCGGRWMCRLRRFIIFFLLILLCLIFLLVLLDYQGMPLVPCPLIPGSSTTS	117	GFLLTRILTIPOSLSWNTSINFLGGTTVCLGQNSQSPTSNHSPTSCPPTCGGRWMCRLRRFIIFFLLILLCLIFLLVLLDYQGMPLVPCPLIPGSSTTS
HBsAg Trans of	2	101	GFLLTRILTIPOSLSWNTSINFLGGTTVCLGQNSQSPTSNHSPTSCPPTCGGRWMCRLRRFIIFFLLILLCLIFLLVLLDYQGMPLVPCPLIPGSSTTS	200	GFLLTRILTIPOSLSWNTSINFLGGTTVCLGQNSQSPTSNHSPTSCPPTCGGRWMCRLRRFIIFFLLILLCLIFLLVLLDYQGMPLVPCPLIPGSSTTS
HBsAg Trans of	3	101	GFLLTRILTIPOSLSWNTSINFLGGTTVCLGQNSQSPTSNHSPTSCPPTCGGRWMCRLRRFIIFFLLILLCLIFLLVLLDYQGMPLVPCPLIPGSSTTS	200	GFLLTRILTIPOSLSWNTSINFLGGTTVCLGQNSQSPTSNHSPTSCPPTCGGRWMCRLRRFIIFFLLILLCLIFLLVLLDYQGMPLVPCPLIPGSSTTS
HBsAg Trans of	4	101	GFLLTRILTIPOSLSWNTSINFLGGTTVCLGQNSQSPTSNHSPTSCPPTCGGRWMCRLRRFIIFFLLILLCLIFLLVLLDYQGMPLVPCPLIPGSSTTS	200	GFLLTRILTIPOSLSWNTSINFLGGTTVCLGQNSQSPTSNHSPTSCPPTCGGRWMCRLRRFIIFFLLILLCLIFLLVLLDYQGMPLVPCPLIPGSSTTS
HBsAg Trans of	Pre	118	AGXCRCTCTTAAQGTSMYPSCCCTKPSDGNCTCIPIPSSWAFGKFLWEWASARFWSLILNPFVQWFGVLSPTVWLSVIMWMWYWGSPSLYSILSPFLPLLP	217	AGXCRCTCTTAAQGTSMYPSCCCTKPSDGNCTCIPIPSSWAFGKFLWEWASARFWSLILNPFVQWFGVLSPTVWLSVIMWMWYWGSPSLYSILSPFLPLLP
HBsAg Trans of	2	201	TGPCRTCMTTAAQGTSMYPSCCCTKPSDGNCTCIPIPSSWAFGKFLWEWASARFWSLILNPFVQWFGVLSPTVWLSVIMWMWYWGSPSLYSILSPFLPLLP	300	TGPCRTCMTTAAQGTSMYPSCCCTKPSDGNCTCIPIPSSWAFGKFLWEWASARFWSLILNPFVQWFGVLSPTVWLSVIMWMWYWGSPSLYSILSPFLPLLP
HBsAg Trans of	3	201	TGPCRTCMTTAAQGTSMYPSCCCTKPSDGNCTCIPIPSSWAFGKFLWEWASARFWSLILNPFVQWFGVLSPTVWLSVIMWMWYWGSPSLYSILSPFLPLLP	300	TGPCRTCMTTAAQGTSMYPSCCCTKPSDGNCTCIPIPSSWAFGKFLWEWASARFWSLILNPFVQWFGVLSPTVWLSVIMWMWYWGSPSLYSILSPFLPLLP
HBsAg Trans of	4	201	AGTCRCTCTTAAQGTSMYPSCCCTKPSDGNCTCIPIPSSWAFGKFLWEWASARFWSLILNPFVQWFGVLSPTVWLSVIMWMWYWGSPSLYSILSPFLPLLP	300	AGTCRCTCTTAAQGTSMYPSCCCTKPSDGNCTCIPIPSSWAFGKFLWEWASARFWSLILNPFVQWFGVLSPTVWLSVIMWMWYWGSPSLYSILSPFLPLLP
HBsAg Trans of	Pre	218	IFFCLWVYI	226	IFFCLWVYI
HBsAg Trans of	2	301	IFFCLWVYI	309	IFFCLWVYI
HBsAg Trans of	3	301	IFFCLWVYI	309	IFFCLWVYI
HBsAg Trans of	4	301	IFFCLWYI	309	IFFCLWYI

Figure 6

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	10	20	30	40	50	
S0						
S6						[SEQ ID NO:20]
S8						[SEQ ID NO:21]
S12	TTTTGGGGAGCCCTCAGGCTCAGGGCATATTACAAACTCTGCCAGCAAAT				T	[SEQ ID NO:22]
S15					TACAAACTTTGCCAGCAAAT	[SEQ ID NO:23]
						[SEQ ID NO:24]

	60	70	80	90	100	
S0						
S6						
S8	GCCCCCTTCTGCCTCCACCAATCGCCAGTCAGGAAGGCAGCCTACCCCGCT					
S12	CCACCTCCTGCCTCCACCAATCGCCAGTCAGGAAGGCAGCCTACCCCGCT					
S15	CCACCTCCTGCCTCCACCAATCGCCAGTCAGGAAGGCAGCCTACCCCGCT					

	110	120	130	140	150	
S0						
S6						
S8	GTCTCCACCTTTGAGAGACACTCATCCTCAGGCCATGCAGTGGAACCTCAA					
S12	GTCTCCACCTTTGAGAGACACTCATCCTCAGGCCATGCAGTGGAACCTCAA					
S15	GTCTCCACCTTTGAGAGACACTCATCCTCAGGCCATGCAGTGGAACCTCAA					

	160	170	180	190	200	
S0						
S6						
S8	CAACCTTCCACCAAACCTCTGCAAGATCCCAGAGTGAAAGGCCTGTATTTTC					
S12	CAACCTTCCACCAAACCTCTGCAAGATCCCAGAGTGAAAGGCCTGTATTTTC					
S15	CAACCTTCCACCAAACCTCTGCAAGATCCCAGAGTGAAAGGCCTGTATTTTC					

	210	220	230	240	250	
S0						
S6						
S8	CCTGCTGGTGGCTCCAGTTCAGGAACAGTAAACCCTGTTCCGACTACTGC					
S12	CCTGCTGGTGGCTCCAGTTCAGGAACAGTAAACCCTGTTCCGACTACTGC					
S15	CCTGCTGGTGGCTCCAGTTCAGGAACAGTAAACCCTGTTCCGACTACTGC					

	260	270	280	290	300	
S0						
S6						
S8	CTCTCACTCATCGTCAATCTTCTCGAGGATTGGGGTCCCTGCGCTGAACA					
S12	CTCTCACTCATCGTCAATCTTCTCGAGGATTGGGGTCCCTGCGCTGAACA					
S15	CTCTCACTCATCGTCAATCTTCTCGAGGATTGGGGTCCCTGCGCTGAACA					

Figure 7

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	310	320	330	340	350
S0					
S6					
S8	TGGAGAACATCACATCAGGACTCCTAGGACCCCTTCTCGTGTTACAGGCG				
S12	TGGAGAACATCACATCAGGACTCCTAGGACCCCTTCTCGTGTTACAGGCG				
S15	TGGAGAACATCACATCAGGACTCCTAGGACCCCTTCTCGTGTTACAGGCG				
	360	370	380	390	400
S0				CGCAGAGTCTAGACTC	
S6					
S8	GGGTTTTTCTTGTTGACAAGAATCCTCACAATACCGCAGAGTCTAGACTC				
S12	GGGTTTTTCTTGTTGACAAGAATCCTCACAATACCGCAGAGTCTAGACTC				
S15	GGGTTTTTCTTGTTGACAAGAATCCTCACAATACCGCAGAGTCTAGACTC				
	410	420	430	440	450
S0	GTGGTGGACTTCTCTCAATTTTCGAGGGGGGACTACCGTGTGTCTTG GCC				
S6					
S8	GTGGTGGACTTCTCTCAATTTTCGAGGGGGGACTACCGTGTGTCTTG GCC				
S12	GTGGTGGACTTCTCTCAATTTTCGAGGGGGGACTACCGTGTGTCTTG GCC				
S15	GTGGTGGACTTCTCTCAATTTTCGAGGGGGGACTACCGTGTGTCTTG GCC				
	460	470	480	490	500
S0	AAAATTTCGAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTCTCTCCA				
S6		TTACTCACCNACCTCCTGTCTCTCCA			
S8	AAAATTTCGAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTCTCTCCA				
S12	AAAATTTCGAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTCTCTCCA				
S15	AAAATTTCGAGTCCCCAACCTCCAATCACTCACCAACCTCCTGTCTCTCCA				
	510	520	530	540	550
S0	ACTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTTATCATCTTCCT				
S6	ACTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTTATCATCTTCCT				
S8	ACTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTTATCATCTTCCT				
S12	ACTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTTATCATCTTCCT				
S15	ACTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTTTATCATCTTCCT				
	560	570	580	590	600
S0	CTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGTTCTTCTGGACTGTC				
S6	CTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGTTCTTCTGGACTGTC				
S8	CTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGTTCTTCTGGACTGTC				
S12	CTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGTTCTTCTGGACTGTC				
S15	CTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGTTCTTCTGGACTGTC				
	610	620	630	640	650
S0	AAGGTATGTTGCCCGTTTGTCTCTAATTCCAGGATCCTCAACCACCAGC				
S6	AAGGTATGTTGCCCGTTTGTCTCTAATTCCAGGATCCTCAACCACCAGC				
S8	AAGGTATGTTGCCCGTTTGTCTCTAATTCCAGGATCCTCAACCACCAGC				
S12	AAGGTATGTTGCCCGTTTGTCTCTAATTCCAGGATCCTCAACCACCAGC				
S15	AAGGTATGTTGCCCGTTTGTCTCTAATTCCAGGATCCTCAACCACCAGC				

Figure 7 (continued)

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	660	670	680	690	700
S0	ACGGGACCATGCCGAACCTGCACGACTCCTGCTCAAGGAACCTCTACGGT				
S6	AGGGGACCATGCCGAACCTGCACGACTCCTGCTCAAGGAACCTCTACGGT				
S8	AGGGGACCATGCCGAACCTGCACGACTCCTGCTCAAGGAACCTCTACGGT				
S12	AGGGGACCATGCCGAACCTGCACGACTCCTGCTCAAGGAACCTCTACGGT				
S15	AGGGGACCATGCCGAACCTGCACGACTCCTGCTCAAGGAACCTCTACGGT				
	710	720	730	740	750
S0	TCCCTCATGTTGCTGTACCAAACCTTCGGACGGAAATTGCACCTGTATTTC				
S6	TCCCTCATGTTGCTGTACCAAACCTTCGGACGGAAATTGCACCTGTATTTC				
S8	TCCCTCATGTTGCTGTACCAAACCTTCGGACGGAAATTGCACCTGTATTTC				
S12	TCCCTCATGTTGCTGTACCAAACCTTCGGACGGAAATTGCACCTGTATTTC				
S15	TCCCTCATGTTGCTGTACCAAACCTTCGGACGGAAATTGCACCTGTATTTC				
	760	770	780	790	800
S0	CCATCCCATCATCCTGGGCTTTTCGGAAAAATTCCTATGGGAGTGGGCCTCA				
S6	CCATCCCATCATCCTGGGCTTTTCGGAAAAATTCCTATGGGAGTGGGCCTCA				
S8	CCATCCCATCATCCTGGGCTTTTCGGAAAAATTCCTATGGGAGTGGGCCTCA				
S12	CCATCCCATCATCCTGGGCTTTTCGGAAAAATTCCTATGGGAGTGGGCCTCA				
S15	CCATCCCATCATCCTGGGCTTTTCGGAAAAATTCCTATGGGAGTGGGCCTCA				
	810	820	830	840	850
S0	GCCCGTTTCTCCTGGCTCAGTTTACTAGTGCCATTTGTTTCAGTGGTTTCGT				
S6	GCCCGTTTCTCCTGGCTCAGTTTACTAGTGCCATTTGTTTCAGTGGTTTCGT				
S8	GCCCGTTTCTCCTGGCTCAGTTTACTAGTGCCATTTGTTTCAGTGGTTTCGT				
S12	GCCCGTTTCTCCTGGCTCAGTTTACTAGTGCCATTTGTTTCAGTGGTTTCGT				
S15	GCCCGTTTCTCCTGGCTCAGTTTACTAGTGCCATTTGTTTCAGTGGTTTCGT				
	860	870	880	890	900
S0	AGGGGCTTTCCCCCACTGTCTGGCTTTTGTATATGGATGATGTGGTATT				
S6	AGGGGCTTTCCCCCACTGTCTGGCTTTTGTATATGGATGATGTGGTATT				
S8	AGGGGCTTTCCCCCACTGTCTGGCTTTTGTATATGGATGATGTGGTATT				
S12	AGGGGCTTTCCCCCACTGTCTGGCTTTTGTATATGGATGATGTGGTATT				
S15	AGGGGCTTTCCCCCACTGTCTGGCTTTTGTATATGGATGATGTGGTATT				
	910	920	930	940	950
S0	GGGGGCCAAGTCTGTATCGCATCTTGAGTCCCTTTTTACCGCTGTTACCA				
S6	GGGGGCCAAGTCTGTATCGCATCTTGAGTCCCTTTTTACCGCTGTTACCA				
S8	GGGGGCCAAGTCTGTATCGCATCTTGAGTCCCTTTTTACCGCTGTTACCA				
S12	GGGGGCCAAGTCTGTATCGCATCTTGAGTCCCTTTTTACCGCTGTTACCA				
S15	GGGGGCCAAGTCTGTATCGCATCTTGAGTCCCTTTTTACCGCTGTTACCA				
	960	970	980	990	1000
S0	ATTTTCTTTTGTCTTTGGGTATACATTTAAACCCTAACAAAACAAAAGA				
S6	ATTTTCTTTTGTCTTTGGGTATACATTTAAATCCTAACAAAACAAAAGA				
S8	ATTTTCTTTTGTCTTTGGGTATACATTTAAATCCTAACAAAACAAAAGA				
S12	ATTTTCTTTTGTCTTTGGGTATACATTTAAATCCTAACAAAACAAAAGA				
S15	ATTTTCTTTTGTCTTTGGGTATACATTTAAATCCTAACAAAACAAAAGA				
	1010	1020	1030	1040	1050

Figure 7 (continued)

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S0 TGGGGTTACTCCCTACATTTTATGGGCTATGTCATTGGAT
S6 TGGGGTTACTCCCTACATTTTATGGGCTATGTCATTGGATGTCATGGGTC
S8 TGGGGTTACTCCCTACATTTTATGGGCTATGTCATTGGATGTCATGGGTC
S12 TGGGGTTACTCCCTACATTTTATGGGCTATGTCATTGGATGTCATGGGTC
S15 TGGGGTTACTCCCTACA

	1060	1070	1080	1090	1100
S0					
S6	CTTGCCACAAGAACACATCAGACAAAAAATCAAAGAATGTTT				AGAAAAC
S8	CTTGCCACAAGAACACATCAGACAAAAAATCA				
S12	CTTGCCACAAGAACACATCAGACAAAAAATCAAAGAATGTTT				AGAAAAC
S15					

Figure 7 (continued)

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Patient B Am

	260	270	280	290	300	
S0	SGHTTNFASKSTSCSLHQSPVRKAAYPAVSTFERHSSSGHAVELNNLPPNS					[SEQ ID NO:25]
S6						[SEQ ID NO:26]
S8	CPFCLHQSPVRKAAYPAVSTFERHSSSGHAVELNNLPPNS					[SEQ ID NO:27]
S12	SGHITNSASKSTSCSLHQSPVRKAAYPAVSTFERHSSSGHAVELNNLPPNS					[SEQ ID NO:28]
S15	TNFASKSTSCSLHQSPVRKAAYPAVSTFERHSSSGHAVELNNLPPNS					[SEQ ID NO:29]

	310	320	330	340	350	
S0	ARSQSERPVFPCWWLQFRNSKPCSDYCLSLIVNLLLEDWGPCEHGEHHIR					
S6						
S8	ARSQSERPVFPCWWLQFRNSKPCSDYCLSLIVNLLLEDWGPCEHGEHHIR					
S12	ARSQSERPVFPCWWLQFRNSKPCSDYCLSLIVNLLLEDWGPCEHGEHHIR					
S15	ARSQSERPVFPCWWLQFRNSKPCSDYCLSLIVNLLLEDWGPCEHGEHHIR					

	360	370	380	390	400	
S0	TPRTPSRVTGGVFLVDKNPHNTAESRLVVDQSFSRGDYRVSWPKFAVPN					
S6						
S8	TPRTPSRVTGGVFLVDKNPHNTAESRLVVDQSFSRGDYRVSWPKFAVPN					
S12	TPRTPSRVTGGVFLVDKNPHNTAESRLVVDQSFSRGDYRVSWPKFAVPN					
S15	TPRTPSRVTGGVFXVDKNPHNTAESRLVVDQSFSRGDYRVSWPKFAVPN					

	410	420	430	440	450	
S0	LQSLTNLLSSNLSWLSLDVSAAFYHLPLHPAAMPHELLVGSSGLSRYVARL					
S6	SNLSWLSLDVSAAFYHLPLHPAAMPHELLVGSSGLSRYVARL					
S8	LQSLTNLLSSNLSWLSLDVSAAFYHLPLHPAAMPHELLVGSSGLSRYVARL					
S12	LQSLTNLLSSNLSWLSLDVSAAFYHLPLHPAAMPHELLVGSSGLSRYVARL					
S15	LQSLTNLLSSNLSWLSLDVSAAFYHLPLHPAAMPHELLVGSTGLSRYVARL					

	460	470	480	490	500	
S0	SSNSRILNHQHGTMPLNLDSCSRNLYGSLMLLYQTFGRKLHLYSHPIILG					
S6	SSNSRILNHQQGTMPNLHDSCSRNLYGSLMLLYQTFGRKLHLYSHPIILG					
S8	SSNSRILNHQQGTMPNLHDSCSRNLYGSLMLLYQTFGRKLHLYSHPIILG					
S12	SSNSRILNHQQGTMPNLHDSCSRNLYGSLMLLYQTFGRKLHLYSHPIILG					
S15	SSNSRILNHQQGTMPNLHDSCSRNLYGSLMLLYQTFGRKLHLYSHPIILG					

	510	520	530	540	550	
S0	FRKIPMGVGLSPFLLAQFTSAICSVVRRAPPHCLAFSYMDDVVLGAKSVS					
S6	FRKIPMGVGLSPFLMAQFTSAICSVVRRAPPHCLAFGYVDDVVLGAKSVS					
S8	FRKIPMGVGLSPFLMAQFTSAICSVVRRAPPHCLAFGYVDDVVLGAKSVS					
S12	FRKIPMGVGLSPFLMAQFTSAICSVVRRAPPHCLAFGYVDDVVLGAKSVS					
S15	FRKIPMGVGLSPFLMAQFTSAICSVVRRAPPHCLAFGYVDDVVLGAKSVS					

	560	570	580	590	600	
S0	HLESFLTAXTNFLLSLGHIHLNPNKTKRWGYSLHFMGYVIGCHGSKPQEH					
S6	HLESFLTAVTNFLLSLGHIHLNPNKTKRWGYSLHFMGYVIG					
S8	HLESFLTAVTNFLLSLGHIHLNPNKTKRWGYSLHFMGYVIGCHGSLPQEH					
S12	HLESFLTAVTNFLLSLGHIHLNPNKTKRWGYSLHFMGYVIG					
S15	HLESFLTAVTNFLLSLGXHLNPNKTKRWGYSL					

Figure 8

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	10	20	30	40	50	
S0						[SEQ ID NO:30]
S6						[SEQ ID NO:31]
S8						[SEQ ID NO:32]
S12	LGSPQAQGI	LQTLPANPPP	PASTNRQSGR	QPTPLSPPL	LRDTHPQAMQ	WNST [SEQ ID NO:33]
S15		PPPA	TNRQSGRQPT	PLSPPL	LRDTHPQAMQ	WNST [SEQ ID NO:34]
	60	70	80	90	100	
S0						
S6						
S8						
S12	TFHQTLQDPR	VKGLYFPAGG	SSSGTVNPV	PTTASHSSSI	FSRIGVPALNM	
S15	TFHQTLQDPR	VKGLYFPAGG	SSSGTVNPV	PTTASHSSSI	FSRIGVPALNM	
	110	120	130	140	150	
S0			QSLDSWWTS	LNFRGGTTV	CLGQ	
S6						
S8						
S12	ENITSGLLG	PLLVLQAGF	LLTRILTIPQ	SLSWWTS	LNFRGGTTV	CLGQ
S15	ENITSGLLG	PLLVLQAGF	LLTRILTIPQ	SLSWWTS	LNFRGGTTV	CLGQ
	160	170	180	190	200	
S0	NSQSPTS	NHSPTSC	PPTCPGYR	WMCLRRFI	IFLFILL	CLIFLLVLLDCQ
S6			PPTCPGYR	WMCLRRFI	IFLFILL	CLIFLLVLLDCQ
S8			PPTCPGYR	WMCLRRFI	IFLFILL	CLIFLLVLLDCQ
S12	NSQSPTS	NHSPTSC	PPTCPGYR	WMCLRRFI	IFLFILL	CLIFLLVLLDCQ
S15	NSQSPTS	NHSPTSC	PPTCPGYR	WMCLRRFI	IFLFILL	CLIFLLVLLDCQ
	210	220	230	240	250	
S0	GMLPVC	PLIPGS	STTSRG	PCRTCTTP	AQGTSTVP	SCCCTKPSDGNCTCIP
S6	GMLPVC	PLIPGS	STTSRG	PCRTCTTP	AQGTSTVP	SCCCTKPSDGNCTCIP
S8	GMLPVC	PLIPGS	STTSRG	PCRTCTTP	AQGTSTVP	SCCCTKPSDGNCTCIP
S12	GMLPVC	PLIPGS	STTSRG	PCRTCTTP	AQGTSTVP	SCCCTKPSDGNCTCIP
S15	GMLPVC	PLIPGS	STTSRG	PCRTCTTP	AQGTSTVP	SCCCTKPSDGNCTCIP
	260	270	280	290	300	
S0	IPSSWAF	GKFLWE	WASARF	SWLSLL	VPFVQWF	VGLSPTVWLLVIWMMWY
S6	IPSSWAF	GKFLWE	WASARF	SWLSLL	VPFVQWF	VGLSPTVWLLVMWMMWY
S8	IPSSWAF	GKFLWE	WASARF	SWLSLL	VPFVQWF	VGLSPTVWLLVMWMMWY
S12	IPSSWAF	GKFLWE	WASARF	SWLSLL	VPFVQWF	VGLSPTVWLLVMWMMWY
S15	IPSSWAF	GKFLWE	WASARF	SWLSLL	VPFVQWF	VGLSPTVWLLVMWMMWY
	310	320				
S0	GPSLYR	ILSPFL	PLXP	IFFCLW	VYI	
S6	GPSLYR	ILSPFL	PLLP	IFFCLW	VYI	
S8	GPSLYR	ILSPFL	PLLP	IFFCLW	VYI	
S12	GPSLYR	ILSPFL	PLLP	IFFCLW	VYI	
S15	GPSLYR	ILSPFL	PLLP	IFFCLW	VXI	

Figure 9

14/32

10 20 30 40 50 60 70 80 90 100
TACTACAAACCTTGCCAGCAATCCGCCCTCTACCAATCGCCAGTCAGGAAGGCAGCCTACCCCTGTGACTCCACCTTTGAGAAACACTCATCC

110 120 130 140 150 160 170 180 190 200
TCAGGCCATGCAGTGGAACTCCACAAACTTCCACCAGACTTACAAGATCCAGAGTGAAGGCCCTGTATCTCCCTGCTGGTGGCTCCAGTTCAGGAACA

210 220 230 240 250 260 270 280 290 300
GTAAACCCCTGTTCCGACTACTGTCTCTCACACATCGTCAATCTTATCGAGGATTGGGGACCCCTGCACCTGAACATGGAGAACATCACATCAGGATTCCTAG

310 320 330 340 350 360 370 380 390 400
GACCCCTGCTCGTGTACAGGCGGGGTTTTTCTTTGTTGACAAAGAAATCCTCACAAATACCGCAGAGTCTAGACTCGTGGTGGACTTCTCTCAATTTTCTAGG

410 420 430 440 450 460 470 480 490 500
GGGGAACACCGTGTGCCTTGGCCAAATTCGCAGTCCCAACCTCCCAATCACTCACCAACCTCCTGTCTCCAACCTTGCTGTTATCGCTGGATGTGT

510 520 530 540 550 560 570 580 590 600
CTGCGCGGTTTTATCATATTCCTCTTCATCCTGCTGCTATGCCCTCATCTTCTTGTGGTCTCTCTGACTATCAAGGTATGTTGCCCGTTTGCCCTCTAA

610 620 630 640 650 660 670 680 690 700
TTCCAGGATCCTCAACCAGCAGCGGACCATGCAAGAACCTGCAGGACTCCTGCTCAAGGAACCTCTWTGTATCCCTCATGTTGCTGTACCAACCTWC

710 720 730 740 750 760 770 780 790 800
GGMCGSAAATTGCACCTGTATTCCTCCATCCCATCATCTGCGCTTTTCGGAAATTCCTATATGGAGTGGCCCTCAGCCCGTTTCTCTGACTCAGTTTACTA

810 820 830 840 850 860 870 880 890 900
GTGCCATTTGTTCAGTGGTTCGTAGGGCTTTTCCCCCACTGTTTGGCTTTCACTATATGGATGATGTGGTATTTGGGGCCAGGTCTGTACAGCATCGTGA

910 920 930 940 950 960 970 980 990 1000
GGCCCTTTTACCGCTGTATACCAATTTTCTTTTGTCTCTGGGTATACATTTAAACCCCGGACAAACAAAGATGGGGTTACTCTTTACATTTTCATGTGGG

1010 1020 1030
TATGTCAATGGATGTTATGGGTCAATGGCCAC

Figure 10

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10 20 30 40 50 60 70 80 90 100
TTNLASKSACLYQSPVRKAAYPSDSTFEKHSSGHAVELHKLPPNSTRSQSERPVSPCWMLQPFNSKPCSDYCLSHIVNLIEDWGPFCTEHGEHHIRIPR

110 120 130 140 150 160 170 180 190 200
TPARVTGGVFLVDKNPHNTAESRLVVDTSQFSRGDHRVPWPKFAVPNLQSLTNLLSSNLSWLSLDVSAAFYHIPHPAAMPHLLVGSSGLSRYVVARLP

210 220 230 240 250 260 270 280 290 300
SRILNHQHGTMQNLHDSCSRNLV/FVSLMLLYQTF/TGRKILHLYSHPIILGFRKIPMGVGLSPFLITQFTSAICSVVRRAPPHCLAFSYMDDDVVLGARSVQ

310 320 330 340
HREALFTAVTNFLLSLGIHLTPDKTKRWGYSLSLHFMGYVIGCYGSLP

Figure 11

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10 20 30 40 50 60 70 80 90 100
LQTLPANPPASTNRQSGRQPTPLTPPLRNTHPQAMQWNSTNFHRTLQDPRVKGLYLPAGGSSSGTVNPPPTTVSHTSSILSRIGDPALNMENITSGFLG

110 120 130 140 150 160 170 180 190 200
PLLVLQAGFFLLTRILTIPOSLDSWWTSLNFGTTVCLGQNSQSPSTNSHSTSCPPTCPGYRNMCLRRFIPLFILLCLIFLLVLLDYQGMPLPVCPLI

210 220 230 240 250 260 270 280 290 300
PGSSTTGTGRCRTCTTPAQGTSM/LYPSCCCKPS/TAANCTCIPIPSSWAFGKFLNEWASARFS*LSLILVPFVQWFVGLSPVWLSVINMMWYWGPGGLYS

310
IVRPFLLPIFFCLWVYI

Figure 12

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10 20 30 40 50 60 70 80 90 100
 TGGTCACAGTGCACACAGTTCCCTCCTGCTCCACCAATCGGCAGTCAGGGAGGCAGCCTACTCCCATCTCTCCACCTCTAAGAGACAGTCATCCTCA
 110 120 130 140 150 160 170 180 190 200
 GGCCATGGTGGCTCAGCCTGCTGGTGGCTCCAGTTCAGGAAACACTCAACCTGTTCCTCAATATTGGCTCTCACAATCTGGTCAATCTCTCTGGAGGACTGGG
 210 220 230 240 250 260 270 280 290 300
 GACCCTGCGCCGAAACATGGAGAACATCACATCAGGATTCCTAGGACCCCTGCTCGTGTACAGSGGGGTTTTTCTTGTGTGACAAGAAATCCTCAACAATAC
 310 320 330 340 350 360 370 380 390 400
 CGCAGAGTCTAGACTCGTGGTGGACTTCTCTCAGTTTTCTAGGGGGATCACCCGCTGTCTTTGGCCAAAATTCGCAGTCCCAACCTCCCAATCACTCACC
 410 420 430 440 450 460 470 480 490 500
 AACCTCCTGTCTCCCAATTTGACCTGGTTATCGCTGGATATGTCTGCGGCGTTTTTATCATATTCTCTTTCATCTCTGCGCTATGCCCTCATCTCTTATTG
 510 520 530 540 550 560 570 580 590 600
 GTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTCTCTTAATTCAGGATCCACACAACACAGTGGGGACCCCTGCAAAACCTGCACGACTCCTGCTC
 610 620 630 640 650 660 670 680 690 700
 AAGGCAACTCTATGTTTCCCTCATGTTGCTGTACAAAACCTACGGATGGAATTCACCTGTATTCCCATCCCATCATCTTGGGCTTTTCGCAAAATACCT
 710 720 730 740 750 760 770 780 790 800
 ATGGGAGTGGGCCCTCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCCATTTGTTCAGTGATTCGTAGGGCTTTCCCCACACTGTTTGGCTTTCAGCTATA
 810 820 830 840 850 860 870 880
 TTGATGATGTGGTACTGGGGGCCAAGTCTGCACAAACATCTTGAGTCCCTTTATACCGCTGTTACCAATTTTCTTTTGTCTTTGGGTAT

Figure 13

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10 20 30 40 50 60 70 80 90 100
GHSANSSSCLHQSAVREAAAYSHLSTSKRQSSSGHGGSAACWWLQFRNTQPCSQYCLSHLVNLLIEDWGPCAEHGEHHIRIPRTPARVTGGVFLVDKNPHNT
110 120 130 140 150 160 170 180 190 200
AESRLVDFSQFSRGITRVSWPKFAVPNLQSLTNLLSSNLTWLSLDMMSAAFYHIPLHPAAMPHELLIGSSCLSRVYVARLSSNSRIHNNQCGTLQNLHDSCS
210 220 230 240 250 260 270 280 290
RQLYVSLMLLYKTYGWLHLYSHPIILGFRKIPMGVGLSPFLLAQFTSAICSVIRRAFPCHCLAFSYIDDDVVLGAKSAQHLESLEYTAVTNFLLSLG

Figure 14

10 20 30 40 50 60 70 80 90 100
VTVPVPPEASTNRQSGRQPTPISPPLRDSHPQAMVAQPAAGSSSGTLNPVNIASHISSISLRTGDPAPNMENITSGFLGPLLVLQAGFFLLTRILTIP
110 120 130 140 150 160 170 180 190 200
QSLDSWWTSLSLGSPVCLGQNSQSPTSNHSPTSCPPI*PGYRWICLRRFIIFLFIPLCLIFLLVLLDYQGMLPVCPLIPGSTTTSAGPCKTCTTPAQ
210 220 230 240 250 260 270 280 290
GNSMFPSCCCTKPTDGNCTCIPIPSSWAFAKYLWEWASVRFSLSLVPEVQ*FVGLSPTVWLSAILMMWYMGPSLHNILSPFIPILPIFFCLWV

Figure 15

20/32

10 20 30 40 50
TCCTGTCCTCCAATTTGTCCTGGTTATCGCTGGATGTGTCTGCGGCGTTT

60 70 80 90 100
TATGATATTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTATTGGTTC

110 120 130 140 150
TTCTGGATTATCAAGGTATGTTGCCCGTCTGTCCTCTAATTCCAGGATCA

160 170 180 190 200
ACAACAACCAAGTACGGGACCATGCAAAACCAAAACCTGCACGACTCCTGC

210 220 230 240 250
TCAAGGCAACTCTATGTTTCCCTCATGTTGCTGTACAAAACCTACGGATG

260 270 280 290 300
GAAATTGCACCTGTATTCCCATCCCATCGTCCTGGGCTTTCGCAAAATTC

310 320 330 340 350
CTATGGGAGTGGGCCTCAGTCCGTTTCTCTTGGCTCAGTTTACTAGTGCC

360 370 380 390 400
ATTTGTTTCAGTGGTTCGTAGGGCTTTCCCCCACTGTTTGGCTTTCAGCTA

410 420 430 440 450
TATGGATGATGTGGTATTGGGGGCCAAGTCTGTACAGCATCGTGAGGCCC

460 470 480 490 500
TTTATACAGCTGTTACCAATTTTCTTTTGTCTCTGGGTATACATTTAAAC

510 520 530 540 550
CCTAACAAAACAAAAGATGGGGTTATTCCCTAAACTTCATGGGTACAT

560 570 580 590
AATTGGAAGTTGGGGAACATTGCCACAGGATCATATTGTAC

Figure 16

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10 20 30 40 50
SNLSWLSLDVSAAFYDIPLHPAAMPHLLIGSSGLSRYVARLSSNSRINNN
60 70 80 90 100
QYGTMQNQNLHDSCSRQLYVSLMLLYKTYGWKLHLYSHPIVLGFRKIPMG
110 120 130 140 150
VGLSPFLLAQFTSAICSVVRRAPPHCLAFSYMDDVVLGAKSVQHREALYT
160 170 180
AVTNFLLSLGIHLNPNKTKRWGYSLNFMGYIIGSWG

Figure 17

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10 20 30 40 50
SCPPICPGYRWMCLRRFMIFLLCLIFLLVLLDYQGMLPVCPLIPGS
60 70 80 90 100
TTTSTGPKTKTKCTTPAQGNSMFPSCCCTKPTDGNCTCIPIPSSWAFKF
110 120 130 140 150
LWEWASVRFSWLSLLVPFVQWFVGLSPTVWLSAIWMMWYWGPSLYSIVRP
160
FIQLLPFIFFCLWVYI

Figure 18

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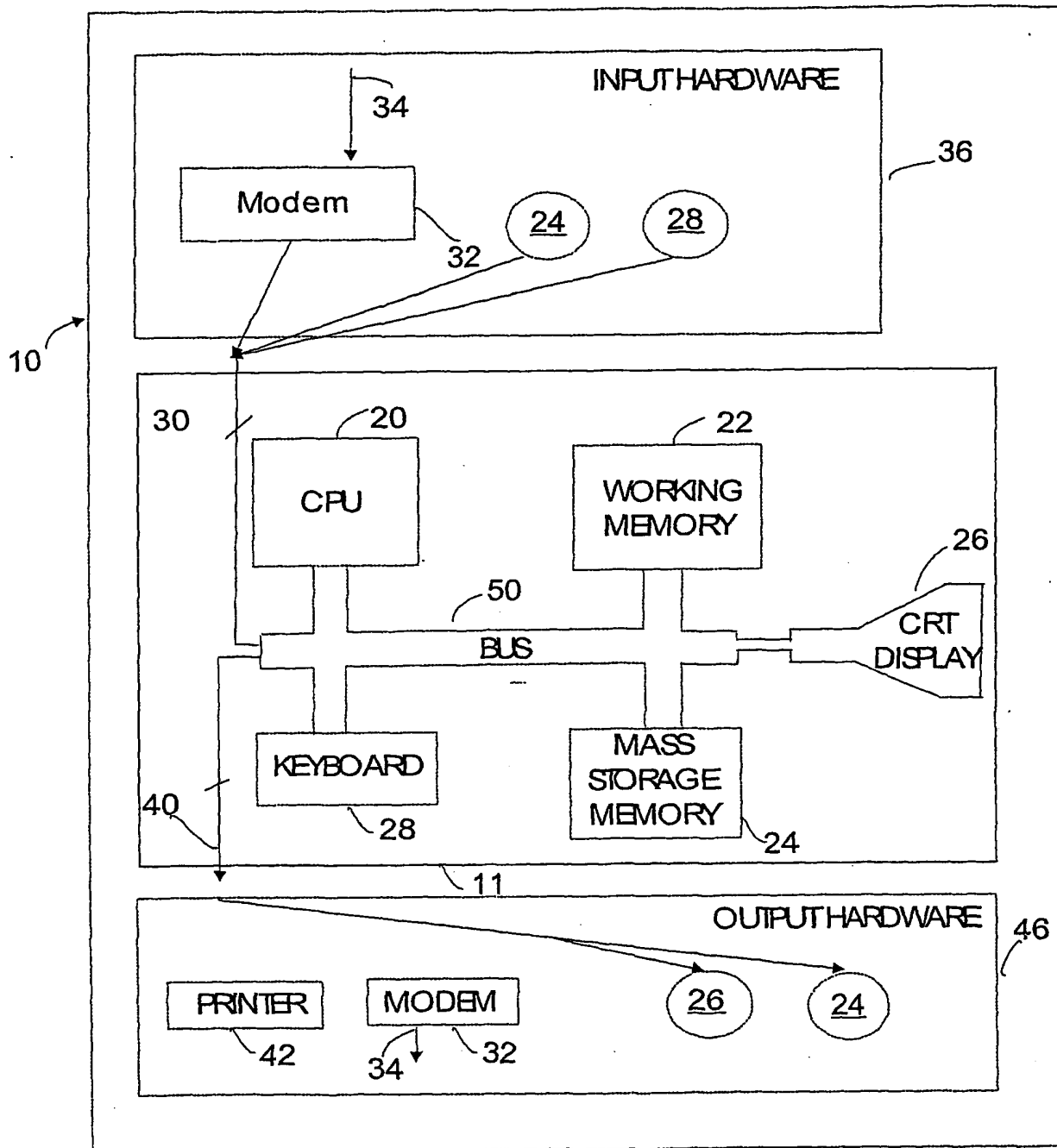


Figure 19

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10 20 30 40 50
AATCCTCACAATACCGCAGAGTCTAGACTTCGTGGTGACTTCTCTCAATT

60 70 80 90 100
TTCTAGGGGACCACCCGTGTGTCTTGGCCAAAATTCGCAGTCCCCAACCT

110 120 130 140 150
CCAATCACTCACCAACCTCTTGTCTCCAATTTGTCCTGGTTATCGCTGG

160 170 180 190 200
ATGTGTCTGCGGCGTTTTATCATATCCCTCTTCATCCTGCTGCTATGCCT

210 220 230 240 250
CATCTTCTTATTGGTTCTTCTGGATTATCAAGGTATGTTGCCCGTTTGTC

260 270 280 290 300
CTCTAATTCCAGGATCCACAACAACCAGTACGGGACCCTGCAAAACCTGC

310 320 330 340 350
ACGACTCCTGCTCAAGGCAACTCTATGTTTCCCTCATGTTGCTGTACAAA

360 370 380 390 400
ACCTACGGATGGAAATTGCACMTGTATTCCCATCCCATCATCTTGGGCTT

410 420 430 440 450
TCGCAAAATACCTATGGGAGTGGGCCTCAGTCCGTTTCTCTTGGTTTCAGT

460 470 480 490 500
TTACTAGTGCCATTTGTTTCAGTGGTTCGTAGGGCTTTCCCCCACTGTTTG

510 520 530 540 550
GCTTTCAGCTATATGGATGATATTGTACTGGGGGCCAAGTCTGTACAACA

560 570 580 590 600
TCTTGAGTCCCTTTATACCGCTGTTACCAATTTCTTTTGTCTTTGGGTA

610 620 630 640 650
TACATTTAACCCTAACAAAACAAAGAGATGGGGTTATTCCTGAATTTTC

660
ATGGGTTATGTAATTGGAA

Figure 20

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10 20 30 40 50
SNLSWLSLDVSAAFYHIPLHPAAMPHLLIGSSGLSRYVARLSSNSRIHNN

60 70 80 90 100
QYGTLONLHDSCSRQLYVSLMLLYKTYGWKLHXYSHPIILGFRKIPMGVG

110 120 130 140 150
LSPFLLVQFTSAICSVVRRAPPHCLAFSYMDDIVLGAKSVQHLESlyTAV

160 170 180
TNFLLSLGIHLTPNKTKRWGYSLNFMGYVIG

Figure 21

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10 20 30 40 50
PICPGYRWMCLRRFIISLFILLLLCLIFLLVLLDYQGMLPVCPLIPGSTTT
60 70 80 90 100
STGPCKTCTTPAQGNSMFPSCCCTKPTDGNCTCIPSSWAFAKYLWEWA
110 120 130 140 150
SVRFSWFSLLVPFVQWFVGLSPTVWL₁SAIWMILYWGPSLYNILSPFIPLL
160
PIFFCLWVYI

Figure 22

27/32

10 20 30 40 50
TCCAATTTGTCTGGGTATCGCTGGATGTGTCTGCGGCGTTTTATCATAT

60 70 80 90 100
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110 120 130 140 150
TATCAAGGTATGTTGCCCGTTTGTCTCTACTTCCAGGAACATCAACTAC

160 170 180 190 200
CAGCACGGGACCATGCAAGACCTGCACGACTCCTGCTCAAGGAACCTCTA

210 220 230 240 250
TGTTTCCCTCTTGTTGCTGTACAAAACCTTCGGACGGAAATTGCACTTGT

260 270 280 290 300
ATTCCCATCCCATCGTCTTGGGCTTTCGCAAGATTCTATGGGAGTGGGC

310 320 330 340 350
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360 370 380 390 400
TCGTAGGGCTTTCCCCCACTGTTTGGCTTTCAGTTATATTGATGATGTGG

410 420 430 440 450
TATTGGGGGCCAAGTCTGTACAACATCTTGAATCCCTTTTACCTCTATT

460 470 480 490 500
ACCAATTTTCTTATGTCTTTGGGTATACATTTAAACCCTAAGAAAACCAA

510 520 530 540 550
ACGTTGGGGCTACTCCCTTAACTTCATGGGATATGTAATTGGAAGTTGGG

GTAC

Figure 23

28/32

10 20 30 40 50
SNLSWVSLDVSAAFYHIPLHPAAMPHELLVGSSGLSRYVARLSSTSRNINY

60 70 80 90 100
QHGTMQDLHDSCSRNLYVSLLLLYKTFGRKLHLYSHPIVLGFRKIPMGVG

110 120 130 140 150
LSPFLLAQFTSAICSVVRRAPPHCLAFSYIDDVVLGAKSVQHLESLFTSI

160 170 180
TNFLMSLGIHLNPKKTKRWGYSLNFMGYVIGSWG

Figure 24

29/32

10 20 30 40 50
PICPGYRWMCLRRFIIIFLFILLCLIFLLVLLDYQGMLPVCPLLPGTSTT
60 70 80 90 100
STGPCKTCTTPAQGTSMFPSCCCTKPSDGNCTCIPIPSWAFARFLWEWA
110 120 130 140 150
SVRFSWLXLLVPFVQWFVGLSPTVWLSVILMMWYWGPSLYNILNPFLPLL
160
PIFLCLWVYI

Figure 25

30/32

```

      10      20      30      40      50
CAGCAAATCCGCCTCCTGCCTCTACCAATCGCCAGTCAGGAAGGCAGCCT
      60      70      80      90     100
ACCCCTCTGTCTCCACCTTTGRGAAACACTCATCCTCAGGCCATGCAGTG
      110     120     130     140     150
GAACTCCACAACCTTCCACCAAACCTCTGCWAGATCCCAGAGTGAGAGGCC
      160     170     180     190     200
TGTATTTCCCTGCTGGTGGCTCCAGTTCAGGAACAGTAAACCTGTTCCG
      210     220     230     240     250
ACTTCTGTCTCTCACACATCGTCAATCTTCTCGAGGATTGGGGWCCCTGC
      260     270     280     290     300
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      310     320     330     340     350
TACAGGCGGGGTTTTTCTTGTTGACAAGAATCCTCACAATACCGCAGAGT
      360     370     380     390     400
CTAGACTCGTGGTGGACTTCTCTCAATTTTCTAGGGGGAACCTACCGTGTG
      410     420     430     440     450
TCTTGGCCAAAATTCGCAGTTCCCAACCTCCAATCACTACCAACCTCCT
      460     470     480     490     500
GTCCTCCAACCTTGWCCCTGGTTATCGCTGGATGTRTCTGCGGCGTTTTATC
      510     520     530     540     550
ATCTTCCTCTTCATCCTGCTGCTATGCCTCATCTTCTTGTTGGTTCTTCT
      560     570     580     590     600
GGACTATCAAGGTATGTTGCCCCGTTTGTCTCTARTTCCAGGATCTTCAA
      610     620     630     640     650
CCACCAGCACGGGACCATGCAGAACCTGCACGACTCCTGCTCAAGGAAMC
      660     670     680     690     700
TCTATGAATCCCTCCTGTTGCTGTACCAAACCTTCGGACGGAAATTGCAC
      710     720     730     740     750
CTGTATTCCCATCCCATCATCCTGGGCTTTCGGAAAATTCCTATGGGAGT
      760     770     780     790     800
GGGCCTCAGCCCGTTTCTCCTGRCTCAGTTTACTAGTGCCATTTGTTTCTCAG
      810     820     830     840     850
TGGTTCGTAGGGCTTTCCCCCACTGTTTGGCTTTCAGTTATATGGATGAT
      860     870     880     890     900
GTGGTATTGGGGGCCAAGTCTGTAYMGCATCTTRAGTCCCTTTTTTACCGC
      910     920     930     940     950
TGTTACCAATTTTCTTTTGTCTYTGCGGTATACATTTAAACCTMACAAAA
      960     970     980     990    1000
CAAAAAGATGGGGTTACTCTTTACATTTTCATGGGCTATGTCATTGGATGT
      1010    1020    1030    1040
TATGGGTCATTGCCACAAGATCACATCAGACAGAAAATCAAAGAA

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Figure 26

31/32

10 20 30 40 50
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60 70 80 90 100
VFPCWWLQFRNSKPCSDFLSHIVNLLEDWGPCAEGEHHIRIPRTPARV
110 120 130 140 150
TGGVFLVDKNPHNTAESRLVVDIFSQFSRGNYRVSWPKFAVPNLQSLTNLL
160 170 180 190 200
SSNLXWLSLDVSAAFYHLPLHPAAMPHELLVGSSGLSRYVARLSSXSRIFN
210 220 230 240 250
HQHGTMQNLHDSCSRXLYESLLLLLYQTFGRKLHLYSHPIILGFRKIPMGV
260 270 280 290 300
GLSPFLLXQFTSAICSVVRRAPHCIAFSYMDDVVLGAKSVXHLXSLFTA
310 320 330 340
VTNFLLSLGIHLNPXKTKRWGYSLHFMGYVIGCYGSLPQDHIRQKIKE

Figure 27

32/32

10 20 30 40 50
ANPPPASTNRQSGRQPTPLSPPLXNTHPQAMQWNSTTFHQTLXDPRVRGL

60 70 80 90 100
YFPAGGSSSGTVNPVPTSVSHTSSIFSRIGXPALNMENITSGFLGPLLV

110 120 130 140 150
QAGFFLLTRILTIPQSLDSWWTSLNFLGGTTVCLGQNSQFPTSNHSPTSC

160 170 180 190 200
PPTXPGYRWMXLRRFIIFFLIFLLVLLDYQGMLPVCPLXPSSST

210 220 230 240 250
TSTGPCRTCTTPAQGXSMNPSCCCTKPSDGNCTCIPSSWAFGKFLWEW

260 270 280 290 300
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Figure 28

- 1 -

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Austin and Repatriation Medical Centre (for all States except the US)
Southern Health (for all States except the US)
Bartholomeusz, Angeline (US only)
Locarnini, Stephen (US only)
Ayres, Anna (US only)
Colledge, Danielle (US only)
Sasadeusz, Joseph (US only)
Tillmann, Hans (US only)
Angus, Peter (US only)
Sievert, William (US only)

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<141> 2003-04-11

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Arg Xaa Pro Arg Thr Pro Xaa Arg Val Xaa Gly Gly Val Phe Leu Val
 20 25 30

Asp Lys Asn Pro His Asn Thr Xaa Glu Ser Xaa Leu Xaa Val Asp Phe
 35 40 45

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 20 25 30

Gly Leu Xaa Arg Tyr Val Ala Arg Leu Ser Ser Xaa Ser Xaa Xaa Xaa
 35 40 45

Asn Xaa Gln Xaa Xaa Xaa Xaa Xaa Xaa Leu His Xaa Xaa Cys Ser Arg
 50 55 60

Xaa Leu Tyr Val Ser Leu Xaa Leu Leu Tyr Xaa Thr Xaa Gly Xaa Lys
 65 70 75 80

Leu His Leu Xaa Xaa His Pro Ile Xaa Leu Gly Phe Arg Lys Xaa Pro

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tttttaccgc tgttaccaat tttcttttgt ctttgggtat acatttaaac cctaacaaaa 180
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tttttaccgc tgttaccaat tttcttttgt ctttgggtat acatttaaac cctaacaaaa 180
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Gln Xaa Glu Arg Pro Val Phe Pro Cys Trp Trp Leu Gln Phe Arg Asn
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Ser Lys Pro Cys Ser Asp Tyr Cys Leu Ser His Ile Val Asn Leu Leu
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Glu Asp Trp Gly Pro Cys Ala Glu His Gly Glu His His Ile Arg Ile
 85 90 95

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Pro Arg Thr Pro Xaa Arg Val Thr Gly Gly Val Phe Leu Val Asp Lys
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Asn Pro His Asn Thr Ala Glu Ser Arg Leu Val Val Asp Phe Ser Gln
 115 120 125

Phe Ser Arg Gly Asn Tyr Arg Val Ser Trp Pro Lys Phe Ala Val Pro
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Ser Leu Asp Val Ser Ala Ala Phe Tyr His Leu Pro Leu His Pro Ala
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Ala Met Pro His Leu Leu Val Gly Ser Ser Gly Leu Ser Arg Tyr Val
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Ala Arg Leu Ser Ser Asn Ser Arg Ile Phe Asn His Gln Arg Gly Xaa
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Phe Arg Asn Ser Lys Pro Cys Ser Asp Tyr Cys Leu Ser Leu Ile Val
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85 90 95

Ile Arg Ile Pro Arg Thr Pro Ser Arg Val Thr Gly Gly Val Phe Leu
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Val	Asp	Lys	Asn	Pro	His	Asn	Thr	Ala	Glu	Ser	Arg	Leu	Val	Val	Asp
		115					120					125			

Phe Ser Gln Phe Ser Arg Gly Asn Tyr Arg Val Ser Trp Pro Lys Phe
130 135 140

Ala Val Pro Asn Leu Gln Ser Leu Thr Asn Leu Leu Ser Ser Asn Leu
145 150 155 160

Ser Trp Leu Ser Leu Asp Val Ser Ala Ala Phe Tyr His Leu Pro Leu
165 170 175

- 18 -

His Pro Ala Ala Met Pro His Leu Leu Val Gly Ser Ser Gly Leu Ser
 180 185 190

Arg Tyr Val Ala Arg Leu Ser Ser Asn Ser Arg Ile Leu Asn Asn Gln
 195 200 205

His Gly Thr Met Pro Asp Leu His Asp Tyr Cys Ser Arg Asn Leu Tyr
 210 215 220

Val Ser Leu Leu Leu Leu Tyr Gln Thr Phe Gly Arg Lys Leu His Leu
 225 230 235 240

Tyr Ser His Pro Ile Ile Leu Gly Phe Arg Lys Ile Pro Met Gly Val
 245 250 255

Gly Leu Ser Pro Phe Leu Leu Ala Gln Phe Thr Ser Ala Ile Cys Ser
 260 265 270

Val Val Arg Arg Ala Phe Pro His Cys Leu Ala Phe Ser Tyr Met Asp
 275 280 285

Asp Val Val Leu Gly Ala Lys Ser Val Gln His Leu Glu Ser Leu Phe
 290 295 300

Thr Ala Val Thr Asn Phe Leu Leu Ser Leu Gly Ile His Leu Asn Pro
 305 310 315 320

Asn Lys Thr Lys Arg Trp Gly Tyr Ser Leu Asn Phe Met Gly Tyr Val
 325 330 335

Ile Gly Cys Tyr
 340

<210> 21
 <211> 344
 <212> PRT
 <213> artificial sequence

<220>
 <223> Pol Trans 3

<400> 21

Leu Ala Gln Gly Ile Leu Gln Asn Phe Ala Ser Lys Ser Ala Ser Cys
 1 5 10 15

- 19 -

Leu His Gln Ser Pro Val Arg Lys Ala Ala Tyr Pro Ala Val Ser Thr
 20 25 30

Phe Glu Lys His Ser Ser Ser Gly His Ala Val Glu Phe His Asn Leu
 35 40 45

Pro Pro Asn Ser Ala Arg Ser Gln Ser Glu Arg Pro Val Phe Pro Cys
 50 55 60

Trp Trp Leu Gln Phe Arg Asn Ser Lys Pro Cys Ser Asp Tyr Cys Leu
 65 70 75 80

Ser Leu Ile Val Asn Leu Leu Glu Asp Trp Gly Pro Cys Ala Glu His
 85 90 95

Gly Glu His His Ile Arg Ile Pro Arg Thr Pro Ser Arg Val Thr Gly
 100 105 110

Gly Val Phe Leu Val Asp Lys Asn Pro His Asn Thr Ala Glu Ser Arg
 115 120 125

Leu Val Val Asp Phe Ser Gln Phe Ser Arg Gly Asn Tyr Arg Val Ser
 130 135 140

Trp Pro Lys Phe Ala Val Pro Asn Leu Gln Ser Leu Thr Asn Leu Leu
 145 150 155 160

Ser Ser Asn Leu Ser Trp Leu Ser Leu Asp Val Ser Ala Ala Phe Tyr
 165 170 175

His Leu Pro Leu His Pro Ala Ala Met Pro His Leu Leu Val Gly Ser
 180 185 190

Ser Gly Leu Ser Arg Tyr Val Ala Arg Leu Ser Ser Asn Ser Arg Ile
 195 200 205

Leu Asn Asn Gln His Gly Thr Met Pro Asp Leu His Asp Tyr Cys Ser
 210 215 220

Arg Asn Leu Tyr Val Ser Leu Leu Leu Leu Tyr Gln Thr Phe Gly Arg
 225 230 235 240

Lys Leu His Leu Tyr Ser His Pro Ile Ile Leu Gly Phe Arg Lys Ile
245 250 255

Pro Met Gly Val Gly Leu Ser Pro Phe Leu Leu Ala Gln Phe Thr Ser
260 265 270

Ala Ile Cys Ser Val Val Arg Arg Ala Phe Pro His Cys Leu Ala Phe
275 280 285

Ser Tyr Met Asp Asp Val Val Leu Gly Ala Lys Ser Val Gln His Leu
290 295 300

Glu Ser Leu Phe Thr Ala Val Thr Asn Phe Leu Leu Ser Leu Gly Ile
305 310 315 320

His Leu Asn Pro Asn Lys Thr Lys Arg Trp Gly Tyr Ser Leu Asn Phe
325 330 335

Met Gly Tyr Val Ile Gly Cys Tyr
340

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<210> 22
<211> 336
<212> PRT
<213> artificial sequence
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<220>
<223> Pol Trans 4

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<220>
<221> MISC_FEATURE
<222> (24)..(24)
<223> x =any amino acid
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<400> 22

Ala Ser Lys Ser Ala Ser Ser Ile Tyr Gln Ser Pro Val Gly Thr Ala
1 5 10 15

Ala Tyr Pro Ala Val Ser Thr Xaa Glu Lys His Ser Ser Ser Gly His
20 25 30

Ala Val Glu Leu His Asn Leu Pro Pro Asn Ser Glu Arg Ser Gln Gly
35 40 45

- 21 -

Glu Arg Pro Val Phe Pro Cys Trp Trp Leu Gln Phe Arg Asn Ser Lys
 50 55 60

Pro Cys Ser Asp Tyr Cys Leu Ser His Ile Val Asn Leu Leu Glu Asp
 65 70 75 80

Trp Gly Pro Cys Ala Glu His Gly Glu His His Ile Arg Ile Pro Arg
 85 90 95

Thr Pro Ala Arg Val Thr Gly Gly Val Phe Leu Val Asp Lys Asn Pro
 100 105 110

His Asn Thr Ala Glu Ser Arg Leu Val Val Asp Phe Ser Gln Phe Ser
 115 120 125

Arg Gly Asn Tyr Arg Val Ser Trp Pro Lys Phe Ala Val Pro Asn Leu
 130 135 140

Gln Ser Leu Thr Asn Leu Leu Ser Ser Asn Leu Ser Trp Leu Ser Leu
 145 150 155 160

Asp Val Ser Ala Ala Phe Tyr His Leu Pro Leu His Pro Ala Ala Met
 165 170 175

Pro His Leu Leu Val Gly Ser Ser Gly Leu Ser Arg Tyr Val Ala Arg
 180 185 190

Leu Ser Ser Asn Ser Arg Ile Phe Asn His Gln Arg Gly Asn Met Gln
 195 200 205

Asn Leu His Asp Cys Cys Ser Arg Asn Leu Tyr Val Ser Leu Leu Leu
 210 215 220

Leu Tyr Gln Thr Phe Gly Arg Lys Leu His Leu Tyr Ser His Pro Ile
 225 230 235 240

Ile Leu Gly Phe Arg Lys Ile Pro Met Gly Val Gly Leu Ser Pro Phe
 245 250 255

Leu Leu Ala Gln Phe Thr Ser Ala Ile Cys Ser Val Val Arg Arg Ala
 260 265 270

Phe Pro His Cys Leu Ala Phe Ser Tyr Met Asp Asp Val Val Leu Gly

- 22 -

275

280

285

Ala Lys Ser Val Gln His Leu Glu Ser Leu Phe Thr Ala Val Thr Asn
 290 295 300

Phe Leu Leu Ser Leu Gly Ile His Leu Asn Pro Asn Lys Thr Lys Arg
 305 310 315 320

Trp Gly Tyr Ser Leu Asn Phe Met Gly Tyr Val Ile Gly Trp Tyr Gly
 325 330 335

<210> 23
 <211> 226
 <212> PRT
 <213> artificial sequence

<220>
 <223> HBsAg Trans of Pre 1

<220>
 <221> MISC_FEATURE
 <222> (120)..(120)
 <223> x = any amino acid

<220>
 <221> MISC_FEATURE
 <222> (208)..(208)
 <223> x = any amino acid

<400> 23

Met Glu Asn Ile Thr Ser Gly Phe Leu Gly Pro Leu Leu Val Leu Gln
 1 5 10 15

Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu
 20 25 30

Asp Ser Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Thr Thr Val Cys
 35 40 45

Leu Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser Pro Thr Ser
 50 55 60

Cys Pro Pro Thr Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe
 65 70 75 80

Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe Leu Leu Val
85 90 95

Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu Ile Pro Gly
100 105 110

Ser Ser Thr Thr Ser Ala Gly Xaa Cys Arg Thr Cys Thr Thr Thr Ala
115 120 125

Gln Gly Thr Ser Met Tyr Pro Ser Cys Cys Cys Thr Lys Pro Ser Asp
130 135 140

Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Gly Lys
145 150 155 160

Phe Leu Trp Glu Trp Ala Ser Ala Arg Phe Ser Trp Leu Ser Leu Leu
165 .. 170 175

Val Pro Phe Val Gln Trp Phe Val Gly Leu Ser Pro Thr Val Trp Leu
180 185 190

Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro Ser Leu Tyr Ser Xaa
195 200 205

Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys Leu Trp Val
210 215 220

Tyr Ile
225

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<210> 24
<211> 309
<212> PRT
<213> artificial sequence
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<220>
<223> HBsAg Trans of 2

<400> 24

Pro Pro Pro Ala Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro
1 5 10 15

Leu Ser Pro Pro Leu Arg Asn Thr His Pro Gln Ala Met Gln Trp Asn
20 25 30

- 24 -

Ser Thr Thr Phe His Gln Thr Leu Gln Asp Pro Arg Val Arg Gly Leu
 35 40 45

Tyr Phe Pro Ala Gly Gly Ser Ser Ser Gly Thr Val Asn Pro Val Leu
 50 55 60

Thr Thr Ala Ser Pro Leu Ser Ser Ile Phe Ser Arg Ile Gly Asp Pro
 65 70 75 80

Ala Leu Asn Met Glu Asn Ile Thr Ser Gly Phe Leu Gly Pro Leu Leu
 85 90 95

Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro
 100 105 110

Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Thr
 115 120 125

Thr Val Cys Leu Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser
 130 135 140

Pro Thr Ser Cys Pro Pro Thr Cys Pro Gly Tyr Arg Trp Met Cys Leu
 145 150 155 160

Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe
 165 170 175

Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu
 180 185 190

Ile Pro Gly Ser Ser Thr Thr Ser Thr Gly Pro Cys Arg Thr Cys Met
 195 200 205

Thr Thr Ala Gln Gly Thr Ser Met Tyr Pro Ser Cys Cys Cys Thr Lys
 210 215 220

Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala
 225 230 235 240

Phe Gly Lys Phe Leu Trp Glu Trp Ala Ser Ala Arg Phe Ser Trp Leu
 245 250 255

- 25 -

Ser Leu Leu Val Pro Phe Val Gln Trp Phe Val Gly Leu Ser Pro Thr
 260 265 270

Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro Ser Leu
 275 280 285

Tyr Ser Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys
 290 295 300

Leu Trp Val Tyr Ile
 305

<210> 25
 <211> 309
 <212> PRT
 <213> artificial sequence

<220>
 <223> HBsAg Trans of 3

<400> 25

Pro Pro Pro Ala Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro
 1 5 10 15

Leu Ser Pro Pro Leu Arg Asn Thr His Pro Gln Ala Met Gln Trp Asn
 20 25 30

Ser Thr Thr Phe His Gln Thr Leu Gln Asp Pro Arg Val Arg Gly Leu
 35 40 45

Tyr Phe Pro Ala Gly Gly Ser Ser Ser Gly Thr Val Asn Pro Val Leu
 50 55 60

Thr Thr Ala Ser Pro Leu Ser Ser Ile Phe Ser Arg Ile Gly Asp Pro
 65 70 75 80

Ala Leu Asn Met Glu Asn Ile Thr Ser Gly Phe Leu Gly Pro Leu Leu
 85 90 95

Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro
 100 105 110

Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Thr
 115 120 125

- 26 -

Thr Val Cys Leu Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser
 130 135 140
 Pro Thr Ser Cys Pro Pro Thr Cys Pro Gly Tyr Arg Trp Met Cys Leu
 145 150 155 160
 Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe
 165 170 175
 Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu
 180 185 190
 Ile Pro Gly Ser Ser Thr Thr Ser Thr Gly Pro Cys Arg Thr Cys Met
 195 200 205
 Thr Thr Ala Gln Gly Thr Ser Met Tyr Pro Ser Cys Cys Cys Thr Lys
 210 215 220
 Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala
 225 230 235 240
 Phe Gly Lys Phe Leu Trp Glu Trp Ala Ser Ala Arg Phe Ser Trp Leu
 245 250 255
 Ser Leu Leu Val Pro Phe Val Gln Trp Phe Val Gly Leu Ser Pro Thr
 260 265 270
 Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro Ser Leu
 275 280 285
 Tyr Ser Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys
 290 295 300
 Leu Trp Val Tyr Ile
 305

<210> 26
 <211> 309
 <212> PRT
 <213> artificial sequence

<220>
 <223> HBsAg Trans of 4

- 27 -

<220>
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 <222> (21)..(21)
 <223> x = any amino acid

<220>
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 <222> (46)..(46)
 <223> x = any amino acid

<400> 26

Pro Pro Pro Pro Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro
 1 5 10 15

Leu Ser Pro Pro Xaa Arg Asn Thr His Pro Gln Ala Met Gln Trp Asn
 20 25 30

Ser Thr Thr Phe His Gln Thr Leu Lys Asp Pro Arg Val Xaa Gly Leu
 35 40 45

Tyr Phe Pro Ala Gly Gly Ser Ser Ser Gly Thr Val Asn Pro Val Pro
 50 55 60

Thr Thr Ala Ser Pro Ile Ser Ser Ile Phe Ser Arg Ile Gly Asp Pro
 65 70 75 80

Ala Leu Asn Met Glu Asn Ile Thr Ser Gly Phe Leu Gly Pro Leu Leu
 85 90 95

Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro
 100 105 110

Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Leu Gly Gly Thr
 115 120 125

Thr Val Cys Leu Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser
 130 135 140

Pro Thr Ser Cys Pro Pro Thr Cys Pro Gly Tyr Arg Trp Met Cys Leu
 145 150 155 160

Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe
 165 170 175

- 28 -

Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu
 180 185 190

Ile Pro Gly Ser Ser Thr Thr Ser Ala Gly Thr Cys Arg Thr Cys Thr
 195 200 205

Thr Ala Ala Gln Gly Thr Ser Met Tyr Pro Ser Cys Cys Cys Thr Lys
 210 215 220

Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala
 225 230 235 240

Phe Gly Lys Phe Leu Trp Glu Trp Ala Ser Ala Arg Phe Ser Trp Leu
 245 250 255

Ser Leu Leu Val Pro Phe Val Gln Trp Phe Val Gly Leu Ser Pro Thr
 260 265 270

Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro Ser Leu
 275 280 285

Tyr Ser Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys
 290 295 300

Leu Trp Ala Tyr Ile
 305

<210> 27
 <211> 656
 <212> DNA
 <213> artificial sequence

<220>
 <223> SO

<220>
 <221> misc_feature
 <222> (561)..(561)
 <223> n = any nucleotide

<400> 27
 cgcagagtct agactcgtgg tggacttctc tcaattttcg aggggggact accgtgtgtc 60
 ttggccaaaa ttgcagtc ccaacctcca atcactcacc aacctcctgt cctccaactt 120
 gtccctgggta tcgctggatg tgtctgcggc gttttatcat cttcctcttc atcctgctgc 180

- 29 -

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tatgcctcat cttcttggtg gttcttctgg actgtcaagg tatgttgccc gtttgcctc 240
taattccagg atcctcaacc accagcacgg gaccatgccg aacctgcacg actcctgctc 300
aaggaacctc tacggttccc tcatgttgct gtaccaaacc ttcggacgga aattgcacct 360
gtattcccat cccatcatcc tgggctttcg gaaaattcct atgggagtgg gcctcagccc 420
gtttctcctg gctcagttta ctagtgccat ttgttcagtg gttagtaggg ctttcccca 480
ctgtctggct tttagttata tggatgatgt ggtattgggg gccaaagtctg tatcgcatct 540
tgagtccttt tttaccgctg ntaccaatth tcttttgtct ttgggtatac atttaaacco 600
taacaaaaca aaaagatggg gttactccct acattttatg ggctatgtca ttggat 656

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<210> 28
<211> 625
<212> DNA
<213> artificial sequence

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<220>
<223> S6

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<220>
<221> misc_feature
<222> (10)..(10)
<223> n = any nucleotide

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<400> 28
ttactcacnn acctcctgtc ctccaacttg tcctgggtat cgctggatgt gtctgcgggc 60
ttttatcatc ttctcttca tcctgctgct atgcctcatc ttcttggttg ttcttctgga 120
ctgtcaaggt atgttgcccc tttgtcctct aattccagga tcctcaacca ccagcagggg 180
accatgccga acctgcacga ctctgctca aggaacctct acggttccct catgttgctg 240
taccaaacct tcggacggaa attgcacctg tattcccatc ccatcatcct gggctttcgg 300
aaaattccta tgggagtggg cctcagcccg tttctcatgg cttagtttac tagtgccatt 360
tgttcagtgg tttagtaggg tttccccac tgtctggctt ttgggttatgt ggatgatgtg 420
gtattggggg ccaagtctgt atcgcatctt ggtcccttt ttaccgctgt taccaattht 480
cttttgtctt tgggtataca tttaaatcct aacaaaacaa aaagatgggg ttactcccta 540
cattttatgg gctatgtcat tggatgtcat gggtccttgc cacaagaaca catcagacaa 600
aaaatcaaag aatgttttag aaaac 625

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<210> 29

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- 30 -

<211> 1033
 <212> DNA
 <213> artificial sequence

<220>
 <223> S8

<400> 29
 tgcccccttct gcctccacca atcgccagtc aggaaggcag cctaccccg cgtctccacc 60
 tttgagagac actcatcctc aggccatgca gtggaactca acaaccttcc accaaactct 120
 gcaagatccc agagtgaag gcctgtatct cctgctggt ggctccagtt caggaacagt 180
 aaacctgtt cgcactactg cctctcactc atcgtaata ttctcgagga ttgggggtccc 240
 tgcgctgaac atggagaaca tcacatcagg actcctagga ccccttctcg tggtacaggc 300
 ggggtttttc ttgttgacaa gaatcctcac aataccgcag agtctagact cgtggtggac 360
 ttctctcaat ttctcgaggg ggactaccgt gtgtcttggc caaaattcgc agtccccaac 420
 ctccaatcac tcaccaacct cctgtcctcc aactgtcct ggttatcgct ggatgtgtct 480
 gggcggtttt atcatcttcc tcttcactct gctgctatgc ctcatcttct tggtggttct 540
 tctggactgt caaggtatgt tgcccgtttg tcctctaatt ccaggatcct caaccaccag 600
 caggggacca tgccgaacct gcacgactcc tgctcaagga acctctacgg ttccctcatg 660
 ttgctgtacc aaaccttcgg acggaaattg cacctgtatt cccatcccat catcctgggc 720
 ttctggaaaa ttcttatggg agtgggcctc agcccgtttc tcatggctca gtttactagt 780
 gccatttggt cagtgggtcg tagggcttcc cccactgtc tggcttttgg ttatgtggat 840
 gatgtggtat tgggggcca gtctgtatcg catcttgagt ccctttttac cgctgttacc 900
 aattttcttt tgtctttggg tatacattta aatcctaaca aaacaaaaag atgggggttac 960
 tccctacatt ttatgggcta tgtcattgga tgtcatgggt ccttgccaca agaacacatc 1020
 agacaaaaaa tca 1033

<210> 30
 <211> 1100
 <212> DNA
 <213> artificial sequence

<220>
 <223> S12

<400> 30
 ttttggggag ccctcaggct cagggcatat tacaaactct gccagcaaat ccacctcctg 60
 cctccaccaa tcgccagtca ggaaggcagc ctaccccgct gtctccacct ttgagagaca 120

- 31 -

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ctcatcctca ggccatgcag tggaactcaa caacottcca ccaaactctg caagatccca      180
gagtgaagg cctgtatttc cctgctggtg gctccagttc aggaacagta aaccctgttc      240
cgactactgc ctctcactca tegtcaatct tctcgaggat tgggggccct gcgctgaaca      300
tggaagaacat cacatcagga ctctaggac ccttctcgt gttacaggcg ggggttttct      360
tggtgacaag aatcctcaca ataccgcaga gtctagactc gtggtggact tctctcaatt      420
ttcgaggggg gactaccgtg tgtcttgcc aaaattcgca gtccccaacc tccaatcact      480
caccaacctc ctgtcctcca acttgctctg gttatcgctg gatgtgtctg cggcgtttta      540
tcattctcct cttcatcctg ctgctatgcc tcattctctt gttggttctt ctggactgtc      600
aaggatatgt gcccgtttgt cctctaattc caggatcctc aaccaccagc aggggaccat      660
gccgaacctg cagactcct gctcaaggaa cctctacggt tccctcatgt tgctgtacca      720
aaccttcgga cggaattgc acctgtattc ccattccatc atcctgggct ttcggaaaat      780
tcctatggga gtgggcctca gcccgtttct catggctcag ttactagtgc ccatttggtc      840
agtggttcgt agggctttcc ccactgtct ggcttttggt tatgtggatg atgtggtatt      900
gggggccaaag tctgtatcgc atcttgagtc cctttttacc gctgttacca attttctttt      960
gtctttgggt atacatttaa atcctaacaa aacaaaaaga tgggggttact ccctacattt    1020
tatgggctat gtcattggat gtcattgggc cttgccacaa gaacacatca gacaaaaaat    1080
caaagaatgt ttagaaaac                                                    1100

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<210> 31
<211> 987
<212> DNA
<213> artificial sequence

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<220>
<223> S15

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<220>
<221> misc_feature
<222> (329)..(329)
<223> y = any nucleotide

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<220>
<221> misc_feature
<222> (943)..(943)
<223> y = any nucleotide

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<400> 31

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- 32 -

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ctacccccgct gtctccacct ttgagagaca ctcatcctca ggccatgcag tggaactcaa	120
caaccttcca ccaaactctg caagatccca gaggtaaagg cctgtatttc cctgctgggtg	180
gtccagttc aggaacagta aaccctgttc cgactactgc ctctcactca tcgtcaatct	240
tctcgaggat tggggtcctt ggcgtgaaca tggagaacat cacatcagga ctctaggac	300
cccttctcgt gttacaggcg ggggttttct tgttgacaag aatcctcaca atacgcaga	360
gtctagactc gtgggtggact tctctcaatt ttcgaggggg gactaccgtg tgtcttggcc	420
aaaattcgca gtccccaacc tccaatcact caccaacctc ctgtcctcca acttgtcctg	480
gttatcgctg gatgtgtctg cggcgtttta tcatcttctt ctccatcctg ctgctatgcc	540
tcatcttctt gttggctcta ctggactgtc aaggatgtt gcccgtttgt cctctaattc	600
caggatcctc aaccaccagc aggggaccat gccgaacctg cagactcct gctcaaggaa	660
cctctacggc tccctcatgt tgctgtacca aagcttcgga cggaaattgc acctgtattc	720
ccatcccatc atcctgggct ttcggaaaat tcctatggga gtgggcctca gcccgtttct	780
catggctcag ttactagtg ccatttgctc agtggttcgt agggctttcc cccactgtct	840
ggcttttggc tatgtggatg atgtggtatt gggggccaag tctgtatcgc atcttgagtc	900
cctttttacc gctgttacca attttcttt gtctttgggt atrcatttaa atcctaacia	960
aacaaaaaga tgggggttact ccctaca	987

<210> 32
 <211> 350
 <212> PRT
 <213> artificial sequence

<220>
 <223> Pol Trans S0

<220>
 <221> MISC_FEATURE
 <222> (309)..(309)
 <223> x = any amino acid

<220>
 <221> MISC_FEATURE
 <222> (345)..(345)
 <223> x = any amino acid

<400> 32

- 33 -

Ser Gly His Thr Thr Asn Phe Ala Ser Lys Ser Thr Ser Cys Leu His
 1 5 10 15

Gln Ser Pro Val Arg Lys Ala Ala Tyr Pro Ala Val Ser Thr Phe Glu
 20 25 30

Arg His Ser Ser Ser Gly His Ala Val Glu Leu Asn Asn Leu Pro Pro
 35 40 45

Asn Ser Ala Arg Ser Gln Ser Glu Arg Pro Val Phe Pro Cys Trp Trp
 50 55 60

Leu Gln Phe Arg Asn Ser Lys Pro Cys Ser Asp Tyr Cys Leu Ser Leu
 65 70 75 80

Ile Val Asn Leu Leu Glu Asp Trp Gly Pro Cys Ala Glu His Gly Glu
 85 90 95

His His Ile Arg Thr Pro Arg Thr Pro Ser Arg Val Thr Gly Gly Val
 100 105 110

Phe Leu Val Asp Lys Asn Pro His Asn Thr Ala Glu Ser Arg Leu Val
 115 120 125

Val Asp Phe Ser Gln Phe Ser Arg Gly Asp Tyr Arg Val Ser Trp Pro
 130 135 140

Lys Phe Ala Val Pro Asn Leu Gln Ser Leu Thr Asn Leu Leu Ser Ser
 145 150 155 160

Asn Leu Ser Trp Leu Ser Leu Asp Val Ser Ala Ala Phe Tyr His Leu
 165 170 175

Pro Leu His Pro Ala Ala Met Pro His Leu Leu Val Gly Ser Ser Gly
 180 185 190

Leu Ser Arg Tyr Val Ala Arg Leu Ser Ser Asn Ser Arg Ile Leu Asn
 195 200 205

His Gln His Gly Thr Met Pro Asn Leu His Asp Ser Cys Ser Arg Asn
 210 215 220

Leu Tyr Gly Ser Leu Met Leu Leu Tyr Gln Thr Phe Gly Arg Lys Leu

225 230 235 240

Asn His Gln Gln Gly Thr Met Pro Asn Leu His Asp Ser Cys Ser Arg
50 55 60

- 35 -

Asn Leu Tyr Gly Ser Leu Met Leu Leu Tyr Gln Thr Phe Gly Arg Lys
 65 70 75 80

Leu His Leu Tyr Ser His Pro Ile Ile Leu Gly Phe Arg Lys Ile Pro
 85 90 95

Met Gly Val Gly Leu Ser Pro Phe Leu Met Ala Gln Phe Thr Ser Ala
 100 105 110

Ile Cys Ser Val Val Arg Arg Ala Phe Pro His Cys Leu Ala Phe Gly
 115 120 125

Tyr Val Asp Asp Val Val Leu Gly Ala Lys Ser Val Ser His Leu Glu
 130 135 140

Ser Leu Phe Thr Ala Val Thr Asn Phe Leu Leu Ser Leu Gly Ile His
 145 150 155 160

Leu Asn Pro Asn Lys Thr Lys Arg Trp Gly Tyr Ser Leu His Phe Met
 165 170 175

Gly Tyr Val Ile Gly
 180

<210> 34
 <211> 340
 <212> PRT
 <213> artificial sequence

<220>
 <223> Pol Trans S8

<400> 34

Cys Pro Phe Cys Leu His Gln Ser Pro Val Arg Lys Ala Ala Tyr Pro
 1 5 10 15

Ala Val Ser Thr Phe Glu Arg His Ser Ser Ser Gly His Ala Val Glu
 20 25 30

Leu Asn Asn Leu Pro Pro Asn Ser Ala Arg Ser Gln Ser Glu Arg Pro
 35 40 45

Val Phe Pro Cys Trp Trp Leu Gln Phe Arg Asn Ser Lys Pro Cys Ser
 50 55 60

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Asp Tyr Cys Leu Ser Leu Ile Val Asn Leu Leu Glu Asp Trp Gly Pro
 65 70 75 80

Cys Ala Glu His Gly Glu His His Ile Arg Thr Pro Arg Thr Pro Ser
 85 90 95

Arg Val Thr Gly Gly Val Phe Leu Val Asp Lys Asn Pro His Asn Thr
 100 105 110

Ala Glu Ser Arg Leu Val Val Asp Phe Ser Gln Phe Ser Arg Gly Asp
 115 120 125

Tyr Arg Val Ser Trp Pro Lys Phe Ala Val Pro Asn Leu Gln Ser Leu
 130 135 140

Thr Asn Leu Leu Ser Ser Asn Leu Ser Trp Leu Ser Leu Asp Val Ser
 145 150 155 160

Ala Ala Phe Tyr His Leu Pro Leu His Pro Ala Ala Met Pro His Leu
 165 170 175

Leu Val Gly Ser Ser Gly Leu Ser Arg Tyr Val Ala Arg Leu Ser Ser
 180 185 190

Asn Ser Arg Ile Leu Asn His Gln Gln Gly Thr Met Pro Asn Leu His
 195 200 205

Asp Ser Cys Ser Arg Asn Leu Tyr Gly Ser Leu Met Leu Leu Tyr Gln
 210 215 220

Thr Phe Gly Arg Lys Leu His Leu Tyr Ser His Pro Ile Ile Leu Gly
 225 230 235 240

Phe Arg Lys Ile Pro Met Gly Val Gly Leu Ser Pro Phe Leu Met Ala
 245 250 255

Gln Phe Thr Ser Ala Ile Cys Ser Val Val Arg Arg Ala Phe Pro His
 260 265 270

Cys Leu Ala Phe Gly Tyr Val Asp Asp Val Val Leu Gly Ala Lys Ser
 275 280 285

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Val Ser His Leu Glu Ser Leu Phe Thr Ala Val Thr Asn Phe Leu Leu
 290 295 300

Ser Leu Gly Ile His Leu Asn Pro Asn Lys Thr Lys Arg Trp Gly Tyr
 305 310 315 320

Ser Leu His Phe Met Gly Tyr Val Ile Gly Cys His Gly Ser Leu Pro
 325 330 335

Gln Glu His Ile
 340

<210> 35
 <211> 340
 <212> PRT
 <213> artificial sequence

<220>
 <223> Pol Trans S12

<400> 35

Ser Gly His Ile Thr Asn Ser Ala Ser Lys Ser Thr Ser Cys Leu His
 1 5 10 15

Gln Ser Pro Val Arg Lys Ala Ala Tyr Pro Ala Val Ser Thr Phe Glu
 20 25 30

Arg His Ser Ser Ser Gly His Ala Val Glu Leu Asn Asn Leu Pro Pro
 35 40 45

Asn Ser Ala Arg Ser Gln Ser Glu Arg Pro Val Phe Pro Cys Trp Trp
 50 55 60

Leu Gln Phe Arg Asn Ser Lys Pro Cys Ser Asp Tyr Cys Leu Ser Leu
 65 70 75 80

Ile Val Asn Leu Leu Glu Asp Trp Gly Pro Cys Ala Glu His Gly Glu
 85 90 95

His His Ile Arg Thr Pro Arg Thr Pro Ser Arg Val Thr Gly Gly Val
 100 105 110

Phe Leu Val Asp Lys Asn Pro His Asn Thr Ala Glu Ser Arg Leu Val
 115 120 125

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Val Asp Phe Ser Gln Phe Ser Arg Gly Asp Tyr Arg Val Ser Trp Pro
 130 135 140

Lys Phe Ala Val Pro Asn Leu Gln Ser Leu Thr Asn Leu Leu Ser Ser
 145 150 155 160

Asn Leu Ser Trp Leu Ser Leu Asp Val Ser Ala Ala Phe Tyr His Leu
 165 170 175

Pro Leu His Pro Ala Ala Met Pro His Leu Leu Val Gly Ser Ser Gly
 180 185 190

Leu Ser Arg Tyr Val Ala Arg Leu Ser Ser Asn Ser Arg Ile Leu Asn
 195 200 205

His Gln Gln Gly Thr Met Pro Asn Leu His Asp Ser Cys Ser Arg Asn
 210 215 220

Leu Tyr Gly Ser Leu Met Leu Leu Tyr Gln Thr Phe Gly Arg Lys Leu
 225 230 235 240

His Leu Tyr Ser His Pro Ile Ile Leu Gly Phe Arg Lys Ile Pro Met
 245 250 255

Gly Val Gly Leu Ser Pro Phe Leu Met Ala Gln Phe Thr Ser Ala Ile
 260 265 270

Cys Ser Val Val Arg Arg Ala Phe Pro-His Cys Leu Ala Phe Gly Tyr
 275 280 285

Val Asp Asp Val Val Leu Gly Ala Lys Ser Val Ser His Leu Glu Ser
 290 295 300

Leu Phe Thr Ala Val Thr Asn Phe Leu Leu Ser Leu Gly Ile His Leu
 305 310 315 320

Asn Pro Asn Lys Thr Lys Arg Trp Gly Tyr Ser Leu His Phe Met Gly
 325 330 335

Tyr Val Ile Gly
 340

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<210> 36
 <211> 328
 <212> PRT
 <213> artificial sequence

<220>
 <223> Pol Trans S15

<220>
 <221> MISC_FEATURE
 <222> (110)..(110)
 <223> x = any amino acid

<220>
 <221> MISC_FEATURE
 <222> (314)..(314)
 <223> x = any amino acid

<400> 36

Thr Asn Phe Ala Ser Lys Ser Thr Ser Cys Leu His Gln Ser Pro Val
 1 5 10 15

Arg Lys Ala Ala Tyr Pro Ala Val Ser Thr Phe Glu Arg His Ser Ser
 20 25 30

Ser Gly His Ala Val Glu Leu Asn Asn Leu Pro Pro Asn Ser Ala Arg
 35 40 45

Ser Gln Ser Glu Arg Pro Val Phe Pro Cys Trp Trp Leu Gln Phe Arg
 50 55 60

Asn Ser Lys Pro Cys Ser Asp Tyr Cys Leu Ser Leu Ile Val Asn Leu
 65 70 75 80

Leu Glu Asp Trp Gly Pro Cys Ala Glu His Gly Glu His His Ile Arg
 85 90 95

Thr Pro Arg Thr Pro Ser Arg Val Thr Gly Gly Val Phe Xaa Val Asp
 100 105 110

Lys Asn Pro His Asn Thr Ala Glu Ser Arg Leu Val Val Asp Phe Ser
 115 120 125

Gln Phe Ser Arg Gly Asp Tyr Arg Val Ser Trp Pro Lys Phe Ala Val
 130 135 140

- 40 -

Pro Asn Leu Gln Ser Leu Thr Asn Leu Leu Ser Ser Asn Leu Ser Trp
 145 150 155 160
 Leu Ser Leu Asp Val Ser Ala Ala Phe Tyr His Leu Pro Leu His Pro
 165 170 175
 Ala Ala Met Pro His Leu Leu Val Gly Ser Thr Gly Leu Ser Arg Tyr
 180 185 190
 Val Ala Arg Leu Ser Ser Asn Ser Arg Ile Leu Asn His Gln Gln Gly
 195 200 205
 Thr Met Pro Asn Leu His Asp Ser Cys Ser Arg Asn Leu Tyr Gly Ser
 210 215 220
 Leu Met Leu Leu Tyr Gln Thr Phe Gly Arg Lys Leu His Leu Tyr Ser
 225 230 235 240
 His Pro Ile Ile Leu Gly Phe Arg Lys Ile Pro Met Gly Val Gly Leu
 245 250 255
 Ser Pro Phe Leu Met Ala Gln Phe Thr Ser Ala Ile Cys Ser Val Val
 260 265 270
 Arg Arg Ala Phe Pro His Cys Leu Ala Phe Gly Tyr Val Asp Asp Val
 275 280 285
 Val Leu Gly Ala Lys Ser Val Ser His Leu Glu Ser Leu Phe Thr Ala
 290 295 300
 Val Thr Asn Phe Leu Leu Ser Leu Gly Xaa His Leu Asn Pro Asn Lys
 305 310 315 320
 Thr Lys Arg Trp Gly Tyr Ser Leu
 325

<210> 37
 <211> 197
 <212> PRT
 <213> artificial sequence

<220>
 <223> HBsAg Trans of S0

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<220>

<221> MISC_FEATURE

<222> (187)..(187)

<223> x = any amino acid

<400> 37

Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Arg Gly Gly Thr
 1 5 10 15

Thr Val Cys Leu Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser
 20 25 30

Pro Thr Ser Cys Pro Pro Thr Cys Pro Gly Tyr Arg Trp Met Cys Leu
 35 40 45

Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe
 50 55 60

Leu Leu Val Leu Leu Asp Cys Gln Gly Met Leu Pro Val Cys Pro Leu
 65 70 75 80

Ile Pro Gly Ser Ser Thr Thr Ser Thr Gly Pro Cys Arg Thr Cys Thr
 85 90 95

Thr Pro Ala Gln Gly Thr Ser Thr Val Pro Ser Cys Cys Cys Thr Lys
 100 105 110

Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala
 115 120 125

Phe Gly Lys Phe Leu Trp Glu Trp Ala Ser Ala Arg Phe Ser Trp Leu
 130 135 140

Ser Leu Leu Val Pro Phe Val Gln Trp Phe Val Gly Leu Ser Pro Thr
 145 150 155 160

Val Trp Leu Leu Val Ile Trp Met Met Trp Tyr Trp Gly Pro Ser Leu
 165 170 175

Tyr Arg Ile Leu Ser Pro Phe Leu Pro Leu Xaa Pro Ile Phe Phe Cys
 180 185 190

Leu Trp Val Tyr Ile

- 42 -

195

<210> 38
 <211> 161
 <212> PRT
 <213> artificial sequence

<220>
 <223> HBsAg Trans of S6

<400> 38

Pro Pro Thr Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile
 1 5 10 15

Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe Leu Leu Val Leu
 20 25 30

Leu Asp Cys Gln Gly Met Leu Pro Val Cys Pro Leu Ile Pro Gly Ser
 35 40 45

Ser Thr Thr Ser Arg Gly Pro Cys Arg Thr Cys Thr Thr Pro Ala Gln
 50 55 60

Gly Thr Ser Thr Val Pro Ser Cys Cys Cys Thr Lys Pro Ser Asp Gly
 65 70 75 80

Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Gly Lys Phe
 85 90 95

Leu Trp Glu Trp Ala Ser Ala Arg Phe Ser Trp Leu Ser Leu Leu Val
 100 105 110

Pro Phe Val Gln Trp Phe Val Gly Leu Ser Pro Thr Val Trp Leu Leu
 115 120 125

Val Met Trp Met Met Trp Tyr Trp Gly Pro Ser Leu Tyr Arg Ile Leu
 130 135 140

Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys Leu Trp Val Tyr
 145 150 155 160

Ile

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<210> 39
 <211> 160
 <212> PRT
 <213> artificial sequence

<220>
 <223> HBsAg Trans of S8

<400> 39

Pro Thr Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile
 1 5 10 15

Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu
 20 25 30

Asp Cys Gln Gly Met Leu Pro Val Cys Pro Leu Ile Pro Gly Ser Ser
 35 40 45

Thr Thr Ser Arg Gly Pro Cys Arg Thr Cys Thr Thr Pro Ala Gln Gly
 50 55 60

Thr Ser Thr Val Pro Ser Cys Cys Cys Thr Lys Pro Ser Asp Gly Asn
 65 70 75 80

Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Gly Lys Phe Leu
 85 90 95

Trp Glu Trp Ala Ser Ala Arg Phe Ser Trp Leu Ser Leu Leu Val Pro
 100 105 110

Phe Val Gln Trp Phe Val Gly Leu Ser Pro Thr Val Trp Leu Leu Val
 115 120 125

Met Trp Met Met Trp Tyr Trp Gly Pro Ser Leu Tyr Arg Ile Leu Ser
 130 135 140

Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys Leu Trp Val Tyr Ile
 145 150 155 160

<210> 40
 <211> 325
 <212> PRT
 <213> artificial sequence

<220>
 <223> HBsAg Trans of S12

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<400> 40

Leu Gly Ser Pro Gln Ala Gln Gly Ile Leu Gln Thr Leu Pro Ala Asn
 1 5 10 15

Pro Pro Pro Ala Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro
 20 25 30

Leu Ser Pro Pro Leu Arg Asp Thr His Pro Gln Ala Met Gln Trp Asn
 35 40 45

Ser Thr Thr Phe His Gln Thr Leu Gln Asp Pro Arg Val Lys Gly Leu
 50 55 60

Tyr Phe Pro Ala Gly Gly Ser Ser Ser Gly Thr Val Asn Pro Val Pro
 65 70 75 80

Thr Thr Ala Ser His Ser Ser Ser Ile Phe Ser Arg Ile Gly Val Pro
 85 90 95

Ala Leu Asn Met Glu Asn Ile Thr Ser Gly Leu Leu Gly Pro Leu Leu
 100 105 110

Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro
 115 120 125

Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Arg Gly Gly Thr
 130 135 140

Thr Val Cys Leu Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser
 145 150 155 160

Pro Thr Ser Cys Pro Pro Thr Cys Pro Gly Tyr Arg Trp Met Cys Leu
 165 170 175

Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe
 180 185 190

Leu Leu Val Leu Leu Asp Cys Gln Gly Met Leu Pro Val Cys Pro Leu
 195 200 205

Ile Pro Gly Ser Ser Thr Thr Ser Arg Gly Pro Cys Arg Thr Cys Thr
 210 215 220

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Thr Pro Ala Gln Gly Thr Ser Thr Val Pro Ser Cys Cys Cys Thr Lys
 225 230 235 240

Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala
 245 250 255

Phe Gly Lys Phe Leu Trp Glu Trp Ala Ser Ala Arg Phe Ser Trp Leu
 260 265 270

Ser Leu Leu Val Pro Phe Val Gln Trp Phe Val Gly Leu Ser Pro Thr
 275 280 285

Val Trp Leu Leu Val Met Trp Met Met Trp Tyr Trp Gly Pro Ser Leu
 290 295 300

Tyr Arg Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys
 305 310 315 320

Leu Trp Val Tyr Ile
 325

<210> 41
 <211> 309
 <212> PRT
 <213> artificial sequence

<220>
 <223> HBsAg Trans of S15

<220>
 <221> MISC_FEATURE
 <222> (308)..(308)
 <223> x = any amino acid

<400> 41

Pro Pro Pro Ala Ser Thr Asn Arg Gln Ser Gly Arg Gln Pro Thr Pro
 1 5 10 15

Leu Ser Pro Pro Leu Arg Asp Thr His Pro Gln Ala Met Gln Trp Asn
 20 25 30

Ser Thr Thr Phe His Gln Thr Leu Gln Asp Pro Arg Val Lys Gly Leu
 35 40 45

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Tyr Phe Pro Ala Gly Gly Ser Ser Ser Gly Thr Val Asn Pro Val Pro
 50 55 60

Thr Thr Ala Ser His Ser Ser Ser Ile Phe Ser Arg Ile Gly Val Pro
 65 70 75 80

Ala Leu Asn Met Glu Asn Ile Thr Ser Gly Leu Leu Gly Pro Leu Leu
 85 90 95

Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr Ile Pro
 100 105 110

Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Arg Gly Gly Thr
 115 120 125

Thr Val Cys Leu Gly Gln Asn Ser Gln Ser Pro Thr Ser Asn His Ser
 130 135 140

Pro Thr Ser Cys Pro Pro Thr Cys Pro Gly Tyr Arg Trp Met Cys Leu
 145 150 155 160

Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe
 165 170 175

Leu Leu Ala Leu Leu Asp Cys Gln Gly Met Leu Pro Val Cys Pro Leu
 180 185 190

Ile Pro Gly Ser Ser Thr Thr Ser Arg Gly Pro Cys Arg Thr Cys Thr
 195 200 205

Thr Pro Ala Gln Gly Thr Ser Thr Val Pro Ser Cys Cys Cys Thr Lys
 210 215 220

Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala
 225 230 235 240

Phe Gly Lys Phe Leu Trp Glu Trp Ala Ser Ala Arg Phe Ser Trp Leu
 245 250 255

Ser Leu Leu Val Pro Phe Val Gln Trp Phe Val Gly Leu Ser Pro Thr
 260 265 270

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Val Trp Leu Leu Val Met Trp Met Met Trp Tyr Trp Gly Pro Ser Leu
 275 280 285

Tyr Arg Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe Phe Cys
 290 295 300

Leu Trp Val Xaa Ile
 305

<210> 42
 <211> 1031
 <212> DNA
 <213> artificial sequence

<220>
 <223> Nucleotide sequence of Patient C

<400> 42
 tactacaaac cttgccagca aatccgcctc ctgcctctac caatcgccag tcaggaaggc 60
 agcctacccc tctgactcca cctttgagaa acactcatcc tcaggccatg cagtggaaact 120
 ccacaaactt ccaccgaact ctacaagatc ccagagtgaaggcctgtat ctccctgctg 180
 gtggctccag ttcaggaaca gtaaaccctg ttccgactac tgtctctcac acatcgtcaa 240
 tcttatcgag gattggggac cctgcactga acatggagaa catcacatca ggattcctag 300
 gacccctgct cgtgttacag gcgggggtttt tottggtgac aagaatcctc acaataccgc 360
 agagtctaga ctcgtggtgg acttctctca attttctagg ggggaccacc gtgtgccttg 420
 gccaaaatc gcagtcccca acctccaatc actcaaccaac ctccctgtcct ccaacttgtc 480
 ctgggttatcg ctggatgtgt ctgcggcggt ttatcatatt cctcttcate ctgctgotat 540
 gcctcatctt cttgttggtt cttctggact atcaagggtat gttgcccgtt tgccctctaa 600
 ttccaggatc ctcaaccacc agcacgggac catgcagaac ctgcacgact cctgctcaag 660
 gaacctctwt gtatccctca tgttgctgta ccaaacctwc ggmcsaaat tgcaacctgta 720
 ttcccatccc atcatcctgg gctttcgga aattcctatg ggagtggggc tcagcccgtt 780
 tctcctgact cagtttacta gtgccatttg ttcagtgggt cgtagggcct tccccactg 840
 tttggctttc agttatatgg atgatgtggt attggggggc aggtctgtac agcatcgtga 900
 ggcccttttt accgctgtta ccaattttct tttgtctctg ggtatacatt taaccccgga 960
 caaaacaaaa agatgggggtt actctttaca tttcatgggc tatgtcattg gatgttatgg 1020
 gtcattgccca c 1031

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<210> 43
 <211> 316
 <212> PRT
 <213> artificial sequence

<220>
 <223> POL Trans of Patient

<400> 43

Thr Thr Asn Leu Ala Ser Lys Ser Ala Ser Cys Leu Tyr Gln Ser Pro
 1 5 10 15

Val Arg Lys Ala Ala Tyr Pro Ser Asp Ser Thr Phe Glu Lys His Ser
 20 25 30

Ser Ser Gly His Ala Val Glu Leu His Lys Leu Pro Pro Asn Ser Thr
 35 40 45

Arg Ser Gln Ser Glu Arg Pro Val Ser Pro Cys Trp Trp Leu Gln Phe
 50 55 60

Arg Asn Ser Lys Pro Cys Ser Asp Tyr Cys Leu Ser His Ile Val Asn
 65 70 75 80

Leu Ile Glu Asp Trp Gly Pro Cys Thr Glu His Gly Glu His His Ile
 85 90 95

Arg Ile Pro Arg Thr Pro Ala Arg Val Thr Gly Gly Val Phe Leu Val
 100 105 110

Asp Lys Asn Pro His Asn Thr Ala Glu Ser Arg Leu Val Val Asp Phe
 115 120 125

Ser Gln Phe Ser Arg Gly Asp His Arg Val Pro Trp Pro Lys Phe Ala
 130 135 140

Val Pro Asn Leu Gln Ser Leu Thr Asn Leu Leu Ser Ser Asn Leu Ser
 145 150 155 160

Trp Leu Ser Leu Asp Val Ser Ala Ala Phe Tyr His Ile Pro Leu His
 165 170 175

Pro Ala Ala Met Pro His Leu Leu Val Gly Ser Ser Gly Leu Ser Arg
 180 185 190

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Tyr Val Ala Arg Leu Pro Ser Asn Ser Arg Ile Leu Asn His Gln His
 195 200 205

Gly Thr Met Gln Asn Leu His Asp Ser Cys Ser Arg Asn Leu Tyr Phe
 210 215 220

Val Ser Leu Met Leu Leu Tyr Gln Thr Phe Thr Gly Arg Lys Leu His
 225 230 235 240

Leu Tyr Ser His Pro Ile Ile Leu Gly Phe Arg Lys Ile Pro Met Gly
 245 250 255

Val Gly Leu Ser Pro Phe Leu Leu Thr Gln Phe Thr Ser Ala Ile Cys
 260 265 270

Ser Ala Leu Phe Thr Ala Val Thr Asn Phe Leu Leu Ser Leu Gly Ile
 275 280 285

His Leu Thr Pro Asp Lys Thr Lys Arg Trp Gly Tyr Ser Leu His Phe
 290 295 300

Met Gly Tyr Val Ile Gly Cys Tyr Gly Ser Leu Pro
 305 310 315

<210> 44
 <211> 301
 <212> PRT
 <213> artificial sequence

<220>
 <223> HBsAg Trans of Patient C

<400> 44

Leu Gln Thr Leu Pro Ala Asn Pro Pro Pro Ala Ser Thr Asn Arg Gln
 1 5 10 15

Ser Gly Arg Gln Pro Thr Pro Leu Thr Pro Pro Leu Arg Asn Thr His
 20 25 30

Pro Gln Ala Met Gln Trp Asn Ser Thr Asn Phe His Arg Thr Leu Gln
 35 40 45

Asp Pro Arg Val Lys Gly Leu Tyr Leu Pro Ala Gly Gly Ser Ser Ser

- 50 -

50

55

60

Gly Thr Val Asn Pro Val Pro Thr Thr Val Ser His Thr Ser Ser Ile
 65 70 75 80

Leu Ser Arg Ile Gly Asp Pro Ala Leu Asn Met Glu Asn Ile Thr Ser
 85 90 95

Gly Phe Leu Gly Pro Leu Leu Val Leu Gln Ala Gly Phe Phe Leu Leu
 100 105 110

Thr Arg Ile Leu Thr Ile Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser
 115 120 125

Leu Asn Phe Leu Gly Gly Thr Thr Val Cys Leu Gly Gln Asn Ser Gln
 130 135 140

Ser Pro Thr Ser Asn His Ser Pro Thr Ser Cys Pro Pro Thr Cys Pro
 145 150 155 160

Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile
 165 170 175

Leu Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly
 180 185 190

Met Leu Pro Val Cys Pro Leu Ile Pro Gly Ser Ser Thr Thr Ser Thr
 195 200 205

Gly Pro Cys Arg Thr Cys Thr Thr Pro Ala Gln Gly Thr Ser Met Leu
 210 215 220

Tyr Pro Ser Cys Cys Cys Thr Lys Pro Ser Thr Ala Ala Asn Cys Thr
 225 230 235 240

Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Gly Lys Phe Leu Trp Glu
 245 250 255

Trp Ala Ser Ala Arg Phe Ser Leu Ser Leu Leu Val Pro Phe Val Gln
 260 265 270

Trp Phe Val Gly Leu Ser Pro Thr Val Trp Leu Ser Val Ile Trp Met
 275 280 285

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Met Trp Tyr Trp Gly Pro Gly Leu Tyr Ser Ile Val Arg
 290 295 300

<210> 45
 <211> 888
 <212> DNA
 <213> artificial sequence

<220>
 <223> Nucleotide sequence of Patient D

<400> 45
 tgggtcacagt gccaacagtt cctcctcctg cctccaccaa tcggcagtca gggaggcagc 60
 ctactcccat ctctccacct ctaagagaca gtcacacctca ggccatgggtg gctcagccctg 120
 ctggtgggtc cagttcagga aactcaacc ctgttcccaa tattgcctct cacatctcgt 180
 caatctcctt gaggactggg gaccctgcgc cgaacatgga gaacatcaca tcaggattcc 240
 taggaccctt gctcgtgtta caggcgggggt ttttcttggt gacaagaatc ctcaacaatac 300
 cgcagagtct agactcgtgg tggacttctc tcagttttct aggggggatca cccgtgtgtc 360
 ttggccaaaa ttgcagtc ccaacctcca atcactcacc aacctcctgt octocaattt 420
 gacctgggta tcgctggata tgtctgcggc gttttatcat attcctcttc atcctgccgc 480
 tatgcctcat cttcttattg gttcttctgg attatcaagg tatgttgccc gtttgtcctc 540
 taattccagg atccacaaca accagtgcgg gacctgcaa aacctgcaag actcctgctc 600
 aaggcaactc tatgtttccc tcatgttgct gtacaaaacc tacggatgga aattgcacct 660
 gtattcccat cccatcatct tgggctttcg caaaatacct atgggagtgg gcctcagtc 720
 gtttctcttg gtcagttta ctagtgccat ttgttcagtg attcgtaggg ctttccccca 780
 ctggttggtt ttcagctata ttgatgatgt ggtactgggg gccaaagtctg cacaacatct 840
 tgagtcctt tataccgctg ttaccaattt tcttttgtct ttgggtat 888

<210> 46
 <211> 295
 <212> PRT
 <213> artificial sequence

<220>
 <223> Pol Trans of Patient D

<400> 46

Gly His Ser Ala Asn Ser Ser Ser Ser Cys Leu His Gln Ser Ala Val

1 5 10 15

Arg Glu Ala Ala Tyr Ser His Leu Ser Thr Ser Lys Arg Gln Ser Ser
20 25 30

Ser Gly His Gly Gly Ser Ala Cys Trp Trp Leu Gln Phe Arg Asn Thr
35 40 45

Gln Pro Cys Ser Gln Tyr Cys Leu Ser His Leu Val Asn Leu Leu Glu
50 55 60

Asp Trp Gly Pro Cys Ala Glu His Gly Glu His His Ile Arg Ile Pro
65 70 75 80

Arg Thr Pro Ala Arg Val Thr Gly Gly Val Phe Leu Val Asp Lys Asn
85 90 95

Pro His Asn Thr Ala Glu Ser Arg Leu Val Val Asp Phe Ser Gln Phe
100 105 110

Ser Arg Gly Ile Thr Arg Val Ser Trp Pro Lys Phe Ala Val Pro Asn
115 120 125

Leu Gln Ser Leu Thr Asn Leu Leu Ser Ser Asn Leu Thr Trp Leu Ser
130 135 140

Leu Asp Met Ser Ala Ala Phe Tyr His Ile Pro Leu His Pro Ala Ala
145 150 155 160

Met Pro His Leu Leu Ile Gly Ser Ser Gly Leu Ser Arg Tyr Val Ala
165 170 175

Arg Leu Ser Ser Asn Ser Arg Ile His Asn Asn Gln Cys Gly Thr Leu
180 185 190

Gln Asn Leu His Asp Ser Cys Ser Arg Gln Leu Tyr Val Ser Leu Met
195 200 205

Leu Leu Tyr Lys Thr Tyr Gly Trp Lys Leu His Leu Tyr Ser His Pro
210 215 220

Ile Ile Leu Gly Phe Arg Lys Ile Pro Met Gly Val Gly Leu Ser Pro
225 230 235 240

- 53 -

Phe Leu Leu Ala Gln Phe Thr Ser Ala Ile Cys Ser Val Ile Arg Arg
 245 250 255

Ala Phe Pro His Cys Leu Ala Phe Ser Tyr Ile Asp Asp Val Val Leu
 260 265 270

Gly Ala Lys Ser Ala Gln His Leu Glu Ser Leu Tyr Thr Ala Val Thr
 275 280 285

Asn Phe Leu Leu Ser Leu Gly
 290 295

<210> 47

<211> 293

<212> PRT

<213> artificial sequence

<220>

<223> HBsAg Trans of Patient D

<400> 47

Val Thr Val Pro Thr Val Pro Pro Pro Ala Ser Thr Asn Arg Gln Ser
 1 5 10 15

Gly Arg Gln Pro Thr Pro Ile Ser Pro Pro Leu Arg Asp Ser His Pro
 20 25 30

Gln Ala Met Val Ala Gln Pro Ala Gly Gly Ser Ser Ser Gly Thr Leu
 35 40 45

Asn Pro Val Pro Asn Ile Ala Ser His Ile Ser Ser Ile Ser Leu Arg
 50 55 60

Thr Gly Asp Pro Ala Pro Asn Met Glu Asn Ile Thr Ser Gly Phe Leu
 65 70 75 80

Gly Pro Leu Leu Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile
 85 90 95

Leu Thr Ile Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Ser Phe
 100 105 110

Leu Gly Gly Ser Pro Val Cys Leu Gly Gln Asn Ser Gln Ser Pro Thr

115

120

125

Ile Cys Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Pro Leu Cys
145 150 155 160

Leu Ile Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val
165 170 175

Cys Pro Leu Ile Pro Gly Ser Thr Thr Thr Ser Ala Gly Pro Cys Lys
180 185 190

Thr Cys Thr Thr Pro Ala Gln Gly Asn Ser Met Phe Pro Ser Cys Cys
195 200 205

Cys Thr Lys Pro Thr Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser
210 215 220

Ser Trp Ala Phe Ala Lys Tyr Leu Trp Glu Trp Ala Ser Val Arg Phe
225 230 235 240

Ser Trp Leu Ser Leu Leu Val Pro Phe Val Gln Phe Val Gly Leu Ser
245 250 255

Pro Thr Val Trp Leu Ser Ala Ile Leu Met Met Trp Tyr Trp Gly Pro
260 265 270

Ser Leu His Asn Ile Leu Ser Pro Phe Ile Pro Leu Leu Pro Ile Phe
275 280 285

Phe Cys Leu Trp Val
290

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<210> 48
<211> 591
<212> DNA
<213> artificial sequence
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<220>
<223> Nucleotide sequence of Patient E

<400> 48

tcctgtcctc caatttgtec tggttatcgc tggatgtgtc tggggcgttt tatgatattc

- 55 -

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ctcttcatcc tgctgctatg cctcatcttc ttattgggtc ttctggatta tcaaggtatg      120
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aaaacctgca cgactcctgc tcaaggcaac tctatgtttc cctcatgttg ctgtacaaaa      240
cctacggatg gaaattgcac ctgtattccc atcccatcgt cctgggcttt cgcaaaattc      300
ctatgggagt gggcctcagt ccgtttctct tggctcagtt tactagtgcc atttgttcag      360
tggttcgtag ggctttcccc cactgtttgg ctttcagcta tatggatgat gtggtattgg      420
gggccaaagtc tgtacagcat cgtgaggccc tttatacagc tgttaccaat tttcttttgt      480
ctctgggtat acatttaaac cctaacaaaa caaaaagatg gggttattcc ctaaacttca      540
tgggttacat aattggaagt tggggaacat tgccacagga tcatattgta c                591

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<210> 49
 <211> 186
 <212> PRT
 <213> artificial sequence

<220>
 <223> Pol Trans of Patient E

<400> 49

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Ser Asn Leu Ser Trp Leu Ser Leu Asp Val Ser Ala Ala Phe Tyr Asp
1              5              10              15

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Ile Pro Leu His Pro Ala Ala Met Pro-His Leu Leu Ile Gly Ser Ser
          20              25              30

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```

Gly Leu Ser Arg Tyr Val Ala Arg Leu Ser Ser Asn Ser Arg Ile Asn
          35              40              45

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Asn Asn Gln Tyr Gly Thr Met Gln Asn Gln Asn Leu His Asp Ser Cys
50              55              60

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Ser Arg Gln Leu Tyr Val Ser Leu Met Leu Leu Tyr Lys Thr Tyr Gly
65              70              75              80

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```

Trp Lys Leu His Leu Tyr Ser His Pro Ile Val Leu Gly Phe Arg Lys
          85              90              95

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```

Ile Pro Met Gly Val Gly Leu Ser Pro Phe Leu Leu Ala Gln Phe Thr
          100              105              110

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- 56 -

Ser Ala Ile Cys Ser Val Val Arg Arg Ala Phe Pro His Cys Leu Ala
 115 120 125

Phe Ser Tyr Met Asp Asp Val Val Leu Gly Ala Lys Ser Val Gln His
 130 135 140

Arg Glu Ala Leu Tyr Thr Ala Val Thr Asn Phe Leu Leu Ser Leu Gly
 145 150 155 160

Ile His Leu Asn Pro Asn Lys Thr Lys Arg Trp Gly Tyr Ser Leu Asn
 165 170 175

Phe Met Gly Tyr Ile Ile Gly Ser Trp Gly
 180 185

<210> 50

<211> 165

<212> PRT

<213> artificial sequence

<220>

<223> HBsAg Trans of Patient E

<400> 50

Ser Cys Pro Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg
 1 5 10 15

Phe Met Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe Leu Leu
 20 25 30

Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu Ile Pro
 35 40 45

Gly Ser Thr Thr Thr Ser Thr Gly Pro Cys Lys Thr Lys Thr Cys Thr
 50 55 60

Thr Pro Ala Gln Gly Asn Ser Met Phe Pro Ser Cys Cys Cys Thr Lys
 65 70 75 80

Pro Thr Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala
 85 90 95

Phe Ala Lys Phe Leu Trp Glu Trp Ala Ser Val Arg Phe Ser Trp Leu
 100 105 110

- 57 -

Ser Leu Leu Val Pro Phe Val Gln Trp Phe Val Gly Leu Ser Pro Thr
 115 120 125

Val Trp Leu Ser Ala Ile Trp Met Met Trp Tyr Trp Gly Pro Ser Leu
 130 135 140

Tyr Ser Ile Val Arg Pro Phe Ile Gln Leu Leu Pro Ile Phe Phe Cys
 145 150 155 160

Leu Trp Val Tyr Ile
 165

<210> 51
 <211> 669
 <212> DNA
 <213> artificial sequence

<220>
 <223> Nucleotide sequence of Patient

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 tgtcctccaa tttgtcctgg ttatcgctgg atgtgtctgc ggcgttttat catatccctc 180
 ttcatcctgc tgctatgcct catcttctta ttggttcttc tggattatca aggtatgttg 240
 cccgtttgtc ctctaattcc aggatccaca acaaccagta cgggaccctg caaaacctgc 300
 acgactcctg ctcaaggcaa ctctatgttt cctcatgtt gctgtacaaa acctacggat 360
 ggaaattgca cmtgtattcc catcccatca tcttgggctt tcgcaaaata cctatgggag 420
 tgggectcag tccgtttctc ttggttcagt ttactagtgc catttgttca gtggttcgta 480
 gggctttccc cactgtttg gctttcagct atatggatga tattgtactg ggggccaaagt 540
 ctgtacaaca tcttgagtcc ctttataaccg ctgttaccaa ttttcttttg tctttgggta 600
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 taattggaa 669

<210> 52
 <211> 181
 <212> PRT
 <213> artificial sequence

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<220>

<223> Deduced sequence of DNA polymerase of Patient F

<220>

<221> MISC_FEATURE

<222> (83)..(83)

<223> x = any amino acid

<400> 52

Ser Asn Leu Ser Trp Leu Ser Leu Asp Val Ser Ala Ala Phe Tyr His
 1 5 10 15

Ile Pro Leu His Pro Ala Ala Met Pro His Leu Leu Ile Gly Ser Ser
 20 25 30

Gly Leu Ser Arg Tyr Val Ala Arg Leu-Ser Ser Asn Ser Arg Ile His
 35 40 45

Asn Asn Gln Tyr Gly Thr Leu Gln Asn Leu His Asp Ser Cys Ser Arg
 50 55 60

Gln Leu Tyr Val Ser Leu Met Leu Leu Tyr Lys Thr Tyr Gly Trp Lys
 65 70 75 80

Leu His Xaa Tyr Ser His Pro Ile Ile Leu Gly Phe Arg Lys Ile Pro
 85 90 95

Met Gly Val Gly Leu Ser Pro Phe Leu Leu Val Gln Phe Thr Ser Ala
 100 105 110

Ile Cys Ser Val Val Arg Arg Ala Phe Pro His Cys Leu Ala Phe Ser
 115 120 125

Tyr Met Asp Asp Ile Val Leu Gly Ala Lys Ser Val Gln His Leu Glu
 130 135 140

Ser Leu Tyr Thr Ala Val Thr Asn Phe Leu Leu Ser Leu Gly Ile His
 145 150 155 160

Leu Thr Pro Asn Lys Thr Lys Arg Trp Gly Tyr Ser Leu Asn Phe Met
 165 170 175

Gly Tyr Val Ile Gly
 180

- 59 -

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<210> 53
 <211> 160
 <212> PRT
 <213> artificial sequence

<220>
 <223> HBsAg Trans of Patient F

<400> 53

Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile
 1 5 10 15

Ser Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu
 20 25 30

Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu Ile Pro Gly Ser Thr
 35 40 45

Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys Thr Thr Pro Ala Gln Gly
 50 55 60

Asn Ser Met Phe Pro Ser Cys Cys Cys Thr Lys Pro Thr Asp Gly Asn
 65 70 75 80

Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Ala Lys Tyr Leu
 85 90 95

Trp Glu Trp Ala Ser Val Arg Phe Ser Trp Phe Ser Leu Leu Val Pro
 100 105 110

Phe Val Gln Trp Phe Val Gly Leu Ser Pro Thr Val Trp Leu Ser Ala
 115 120 125

Ile Trp Met Ile Leu Tyr Trp Gly Pro Ser Leu Tyr Asn Ile Leu Ser
 130 135 140

Pro Phe Ile Pro Leu Leu Pro Ile Phe Phe Cys Leu Trp Val Tyr Ile
 145 150 155 160

<210> 54
 <211> 554
 <212> DNA
 <213> artificial sequence

- 60 -

<220>

<223> Nucleotide sequence of Patient G

<400> 54

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tccaatttgt cctgggtatc gctggatgtg tctgcggcgt tttatcatat tcctcttcat      60
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ttgtcctcta cttccaggaa catcaactac cagcacggga ccatgcaaga cctgcacgac      180
tcctgetcaa ggaacctcta tgtttccctc ttgttgctgt acaaaacctt cggacggaaa      240
ttgcacttgt attcccatcc catcgtcttg ggctttcgca agattcctat gggagtgggc      300
ctcagtcctg ttctcttggc tcartttact agtgccattt gttcagtggg tcgtagggct      360
ttccccact gtttggtttt cagttatatt gatgatgtgg tattgggggc caagtctgta      420
caacatcttg aatccctttt tacctctatt accaattttc ttatgtcttt gggatacat      480
ttaaacccta agaaaaccaa acgttggggc tactccctta acttcatggg atatgtaatt      540
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<210> 55

<211> 184

<212> PRT

<213> artificial sequence

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<223> Deduced sequence of DNA polymerase of Patient G

<400> 55

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Ser Asn Leu Ser Trp Val Ser Leu Asp Val Ser Ala Ala Phe Tyr His
1           5           10           15
Ile Pro Leu His Pro Ala Ala Met Pro His Leu Leu Val Gly Ser Ser
          20           25           30
Gly Leu Ser Arg Tyr Val Ala Arg Leu Ser Ser Thr Ser Arg Asn Ile
          35           40           45
Asn Tyr Gln His Gly Thr Met Gln Asp Leu His Asp Ser Cys Ser Arg
          50           55           60
Asn Leu Tyr Val Ser Leu Leu Leu Tyr Lys Thr Phe Gly Arg Lys
65           70           75           80
Leu His Leu Tyr Ser His Pro Ile Val Leu Gly Phe Arg Lys Ile Pro
          85           90           95

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Met Gly Val Gly Leu Ser Pro Phe Leu Leu Ala Gln Phe Thr Ser Ala
100 105 110

Ile Cys Ser Val Val Arg Arg Ala Phe Pro His Cys Leu Ala Phe Ser
115 120 125

Tyr Ile Asp Asp Val Val Leu Gly Ala Lys Ser Val Gln His Leu Glu
130 135 140

Ser Leu Phe Thr Ser Ile Thr Asn Phe Leu Met Ser Leu Gly Ile His
145 150 155 160

Leu Asn Pro Lys Lys Thr Lys Arg Trp Gly Tyr Ser Leu Asn Phe Met
165 170 175

Gly Tyr Val Ile Gly Ser Trp Gly
180

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<210> 56
<211> 160
<212> PRT
<213> artificial sequence
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<220>
<223> HBsAg Trans of Patient G

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<220>
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<222> (108)..(108)
<223> x = any amino acid
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<400> 56

Pro Ile Cys Pro Gly Tyr Arg Trp Met Cys Leu Arg Arg Phe Ile Ile
1 5 10 15

Phe Leu Phe Ile Leu Leu Leu Cys Leu Ile Phe Leu Leu Val Leu Leu
20 25 30

Asp Tyr Gln Gly Met Leu Pro Val Cys Pro Leu Leu Pro Gly Thr Ser
35 40 45

Thr Thr Ser Thr Gly Pro Cys Lys Thr Cys Thr Thr Pro Ala Gln Gly
50 55 60

- 62 -

Thr Ser Met Phe Pro Ser Cys Cys Cys Thr Lys Pro Ser Asp Gly Asn
65 70 75 80

Cys Thr Cys Ile Pro Ile Pro Ser Ser Trp Ala Phe Ala Arg Phe Leu
85 90 95

Trp Glu Trp Ala Ser Val Arg Phe Ser Trp Leu Xaa Leu Leu Val Pro
100 105 110

Phe Val Gln Trp Phe Val Gly Leu Ser Pro Thr Val Trp Leu Ser Val
115 120 125

Ile Leu Met Met Trp Tyr Trp Gly Pro Ser Leu Tyr Asn Ile Leu Asn
130 135 140

Pro Phe Leu Pro Leu Leu Pro Ile Phe Leu Cys Leu Trp Val Tyr Ile
145 150 155 160

<210> 57
<211> 1045
<212> DNA
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<220>
<223> Nucleotide sequence of Patient H

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aaactctgcw agatccaga gtgagaggcc tgtatttccc tgctgggtggc tccagttcag 180
gaacagtaaa ccctgttccg acttctgtct ctcacacatc gtcaatcttc tcgaggattg 240
gggwcctgc gctgaacatg gagaacatca catcaggatt cctaggaccc ctgctcgtgt 300
tacaggcggg gtttttcttg ttgacaagaa tctcacaat accgcagagt ctagactcgt 360
ggtggacttc tctcaatttt ctagggggaa ctaccgtgtg tcttggccaa aattcgcagt 420
tcccaacctc caatcactca ccaacctcct gtccccaac ttgwcctggg tatcgctgga 480
tgtrtctgcg gcgttttatc atcttcctct tcatcctgct gctatgcctc atcttcttgt 540
tggttcttct ggactatcaa ggtatgttgc ccgtttgtcc tctarttcca ggatcttcaa 600
ccaccagcac gggaccatgc agaacctgca cgactcctgc tcaaggaamc tctatgaatc 660
cctcctgttg ctgtacaaa ccttcggacg gaaattgcac ctgtattccc atcccatcat 720

- 63 -

cctgggcttt cggaaaattc ctatgggagt gggcctcagc ccgtttctcc tgrctcagtt 780
tactagtgcc atttggttcag tgggttcgtag ggctttcccc cactgttttg ctttcagtta 840
tatggatgat gtggtattgg gggccaagtc tgtaymgcat cttragtccc tttttaccgc 900
tgttaccaat tttcttttgt ctytgggtat acatttaaac cctmacaaaa caaaaagatg 960
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tcacatcaga cagaaaatca aagaa 1045

<210> 58
<211> 348
<212> PRT
<213> artificial sequence

<220>
<223> Deduced sequence of DNA polymerase of Patient H

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<223> x = any amino acid

<220>
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- 64 -

<220>
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 <223> x = any amino acid

<220>
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 <223> x = any amino acid

<400> 58

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Tyr Pro Ser Val Ser Thr Phe Xaa Lys His Ser Ser Ser Gly His Ala
 20 25 30

Val Glu Leu His Asn Leu Pro Pro Asn Ser Ala Arg Ser Gln Ser Glu
 35 40 45

Arg Pro Val Phe Pro Cys Trp Trp Leu Gln Phe Arg Asn Ser Lys Pro
 50 55 60

Cys Ser Asp Phe Cys Leu Ser His Ile Val Asn Leu Leu Glu Asp Trp
 65 70 75 80

Gly Pro Cys Ala Glu His Gly Glu His His Ile Arg Ile Pro Arg Thr
 85 90 95

Pro Ala Arg Val Thr Gly Gly Val Phe Leu Val Asp Lys Asn Pro His
 100 105 110

Asn Thr Ala Glu Ser Arg Leu Val Val Asp Phe Ser Gln Phe Ser Arg
 115 120 125

Gly Asn Tyr Arg Val Ser Trp Pro Lys Phe Ala Val Pro Asn Leu Gln
 130 135 140

Ser Leu Thr Asn Leu Leu Ser Ser Asn Leu Xaa Trp Leu Ser Leu Asp
 145 150 155 160

Val Ser Ala Ala Phe Tyr His Leu Pro Leu His Pro Ala Ala Met Pro
 165 170 175

- 65 -

His Leu Leu Val Gly Ser Ser Gly Leu Ser Arg Tyr Val Ala Arg Leu
 180 185 190

Ser Ser Xaa Ser Arg Ile Phe Asn His Gln His Gly Thr Met Gln Asn
 195 200 205

Leu His Asp Ser Cys Ser Arg Xaa Leu Tyr Glu Ser Leu Leu Leu Leu
 210 215 220

Tyr Gln Thr Phe Gly Arg Lys Leu His Leu Tyr Ser His Pro Ile Ile
 225 230 235 240

Leu Gly Phe Arg Lys Ile Pro Met Gly Val Gly Leu Ser Pro Phe Leu
 245 250 255

Leu Xaa Gln Phe Thr Ser Ala Ile Cys Ser Val Val Arg Arg Ala Phe
 260 265 270

Pro His Cys Leu Ala Phe Ser Tyr Met Asp Asp Val Val Leu Gly Ala
 275 280 285

Lys Ser Val Xaa His Leu Xaa Ser Leu Phe Thr Ala Val Thr Asn Phe
 290 295 300

Leu Leu Ser Leu Gly Ile His Leu Asn Pro Xaa Lys Thr Lys Arg Trp
 305 310 315 320

Gly Tyr Ser Leu His Phe Met Gly Tyr Val Ile Gly Cys Tyr Gly Ser
 325 330 335

Leu Pro Gln Asp His Ile Arg Gln Lys Ile Lys Glu
 340 345

<210> 59
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 <212> PRT
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 <222> (24)..(24)

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<223> x = any amino acid

<220>

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<222> (43)..(43)

<223> x = any amino acid

<220>

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<222> (81)..(81)

<223> x = any amino acid

<220>

<221> MISC_FEATURE

<222> (154)..(154)

<223> x = any amino acid

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<222> (161)..(161)

<223> x = any amino acid

<220>

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<222> (195)..(195)

<223> x = any amino acid

<220>

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<222> (216)..(216)

<223> x = any amino acid

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<222> (257)..(257)

<223> x = any amino acid

<220>

<221> MISC_FEATURE

<222> (292)..(292)

<223> x = any amino acid

<400> 59

Ala	Asn	Pro	Pro	Pro	Ala	Ser	Thr	Asn	Arg	Gln	Ser	Gly	Arg	Gln	Pro
1				5					10					15	

- 67 -

Thr Pro Leu Ser Pro Pro Leu Xaa Asn Thr His Pro Gln Ala Met Gln
 20 25 30

Trp Asn Ser Thr Thr Phe His Gln Thr Leu Xaa Asp Pro Arg Val Arg
 35 40 45

Gly Leu Tyr Phe Pro Ala Gly Gly Ser Ser Ser Gly Thr Val Asn Pro
 50 55 60

Val Pro Thr Ser Val Ser His Thr Ser Ser Ile Phe Ser Arg Ile Gly
 65 70 75 80

Xaa Pro Ala Leu Asn Met Glu Asn Ile Thr Ser Gly Phe Leu Gly Pro
 85 90 95

Leu Leu Val Leu Gln Ala Gly Phe Phe Leu Leu Thr Arg Ile Leu Thr
 100 105 110

Ile Pro Gln Ser Leu Asp Ser Trp Trp Thr Ser Leu Asn Phe Leu Gly
 115 120 125

Gly Thr Thr Val Cys Leu Gly Gln Asn Ser Gln Phe Pro Thr Ser Asn
 130 135 140

His Ser Pro Thr Ser Cys Pro Pro Thr Xaa Pro Gly Tyr Arg Trp Met
 145 150 155 160

Xaa Leu Arg Arg Phe Ile Ile Phe Leu Phe Ile Leu Leu Leu Cys Leu
 165 170 175

Ile Phe Leu Leu Val Leu Leu Asp Tyr Gln Gly Met Leu Pro Val Cys
 180 185 190

Pro Leu Xaa Pro Gly Ser Ser Thr Thr Ser Thr Gly Pro Cys Arg Thr
 195 200 205

Cys Thr Thr Pro Ala Gln Gly Xaa Ser Met Asn Pro Ser Cys Cys Cys
 210 215 220

Thr Lys Pro Ser Asp Gly Asn Cys Thr Cys Ile Pro Ile Pro Ser Ser
 225 230 235 240

Trp Ala Phe Gly Lys Phe Leu Trp Glu Trp Ala Ser Ala Arg Phe Ser

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245

250

255

Xaa Leu Ser Leu Leu Val Pro Phe Val Gln Trp Phe Val Gly Leu Ser
260 265 270

Pro Thr Val Trp Leu Ser Val Ile Trp Met Met Trp Tyr Trp Gly Pro
275 280 285

Ser Leu Tyr Xaa Ile Leu Ser Pro Phe Leu Pro Leu Leu Pro Ile Phe
290 295 300

Phe Cys Leu Trp Val Tyr Ile
305 310

a

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU03/00432

A. CLASSIFICATION OF SUBJECT MATTER												
Int. Cl. ⁷ : C12N7/00, 15/01, 15/36, 15/51, C12Q1/70												
According to International Patent Classification (IPC) or to both national classification and IPC												
B. FIELDS SEARCHED												
Minimum documentation searched (classification system followed by classification symbols) SEE BELOW												
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched SEE BELOW												
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) WPIDS, MEDLINE, CA. KEYWORDS: Hepatitis B/Nucleotide/Nucleoside/Resistan?/Muta?/Adefovir/ Lamivudine/Tenofivir/Thiacydidine/HBsAg/Polymcrase and similar terms												
C. DOCUMENTS CONSIDERED TO BE RELEVANT												
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.										
X	WO 01/94559 (Melbourne Health) 13 December 2001 Claims, p.12-19, p.22 line 25- p.24 line 25, and p. 25 line 30 - p. 26 line 9	1-125, 169-202										
X	WO 01/57244 (Melbourne Health) 9 August 2001 Claims, Table 1, p. 17 line 7 - p. 21 line 12 and p. 25 line 16 - p. 33 line 2	1-17, 19-74, 80, 86, 95, 106, 119, 123-127										
☒ Further documents are listed in the continuation of Box C ☒ See patent family annex												
* Special categories of cited documents: <table border="0"> <tr> <td>"A" document defining the general state of the art which is not considered to be of particular relevance</td> <td>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td> </tr> <tr> <td>"E" earlier application or patent but published on or after the international filing date</td> <td>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td> </tr> <tr> <td>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td> <td>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td> </tr> <tr> <td>"O" document referring to an oral disclosure, use, exhibition or other means</td> <td>"&" document member of the same patent family</td> </tr> <tr> <td>"P" document published prior to the international filing date but later than the priority date claimed</td> <td></td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention	"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone	"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art	"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family	"P" document published prior to the international filing date but later than the priority date claimed	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention											
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone											
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art											
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family											
"P" document published prior to the international filing date but later than the priority date claimed												
Date of the actual completion of the international search 27 May 2003		Date of mailing of the international search report 06 JUN 2003										
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustalia.gov.au Facsimile No. (02) 6285 3929		Authorized officer ALISTAIR BESTOW Telephone No : (02) 6283 2450										

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU03/00432

Box I Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos :
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos : 126, 159, 160 (completely), 161-168 (partially)
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
The claims are not restricted to the technical features of the invention, namely hepatitis B variants, methods of using these variants and products of these methods.
Claims 161-168 have only been searched in so far as they relate to HBV nucleic acid or peptides sequences, antibodies, ribozymes and antisense that are capable of inhibiting the variant HBVs of the invention
3. ☐ Claims Nos :
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See Supplemental Box for summary inventions.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98/21317 (Western Health Care Network) 22 May 1998 Claims, p. 4 line 5 - p. 7 line 12 and p. 8 line 28 - p. 11 line 20,	1-17, 19-37, 39, 40, 42-50, 54, 55, 58-74, 76-78, 80-90, 94, 95, 98, 100-114, 118, 119, 122, 170- 178, 180-182, 184-186, 190, 194-202
X	Yeh, C. et al., 2000, <i>Clearance of the original hepatitis B virus YMDD-motif mutants with emergence of distinct lamivudine-resistant mutants during prolonged lamivudine therapy</i> , Hepatology, 31:1318-1325 See whole document	1-17, 19-37, 39, 40, 49, 50, 54, 55, 58-74, 76, 77, 78, 82, 85, 86, 89, 90, 94, 95, 98, 100-102, 106, 109, 113, 114, 118, 119, 122, 127-129
X	Seigneres, B. et al., 2000, <i>Evolution of Hepatitis B virus polymerase gene sequence during famciclovir therapy for chronic hepatitis B</i> , Journal of Infectious Diseases, 181:1221-33 See whole document	1-17, 19-38, 42, 50, 54, 57, 58-74, 80, 85, 86, 90, 97, 104, 109, 110, 114, 118, 121, 122, 127-129
X	Ogata, N. et al., 1999, <i>Novel patterns of amino acid mutations in the hepatitis b virus polymerase in association with resistance to lamivudine therapy in japanese patients with chronic hepatitis B</i> , Journal of Medical Virology, 59:270-276 See whole document	1-17, 19-37, 43, 59-74, 81, 105
X	Bock, C. et al., 2002(February), <i>Selection of hepatitis B virus polymerase mutants with enhanced replication by lamivudine treatment after liver transplantation</i> , Gastroenterology, 122:264-273 See whole document	1-17, 19-37, 39, 44, 54, 55, 58-74, 83, 94, 95, 98, 100, 107, 118, 119, 122

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU03/00432

C (Continuation)

DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Cane, P. et al., 1999, <i>Analysis of hepatitis B virus quasispecies changes during the emergence and reversion of lamivudine resistance in liver transplantation</i>, Antiviral Therapy, 4:7-14 See whole document	1-17, 19-37, 39, 43, 45, 49, 50, 55, 58-74, 81, 84, 86, 89, 90, 94, 95, 98, 100, 102, 108, 110, 113, 114, 118, 119, 122

Supplemental Box

(To be used when the space in any of Boxes I to VIII is not sufficient)

Continuation of Box No II:

Invention 1: Claims 1- 20, 38, 59-75, 99, 123-125, 127, 130-134, 170, 178, 179, 195 (all partially) relating to an isolated Hepatitis B virus (HBV) variant comprising a mutation in a gene encoding DNA polymerase resulting in an amino acid addition, substitution and/or deletion at amino acid position rt21 of the HBV DNA polymerase, the use of these variants, and methods for determining whether a HBV variant exhibits decrease sensitivity to anti-viral agents or reduced interactivity to an antibody to HBV surface antigen.

Invention 2: 1- 20, 38, 59-75, 77, 99, 101, 123-125, 127, 130-134, 136, 170, 178, 179, 181, 195 (all partially) relating to an isolated HBV variant comprising a mutation in a gene encoding DNA polymerase resulting in an amino acid addition, substitution and/or deletion at amino acid position rt122 of the HBV DNA polymerase, the use of these variants, and methods for determining whether a HBV variant exhibits decrease sensitivity to anti-viral agents or reduced interactivity to an antibody to HBV surface antigen.

Inventions 3-37: relating to HBV variants comprising a mutation in a gene encoding DNA polymerase and/or HBsAg resulting in an amino acid addition, substitution and/or deletion at amino acid positions rt124, rt28, rt130, etc, rt251 or the equivalent position in the overlapping HBsAg, the use of these variants, and methods for determining whether a HBV variant exhibits decrease sensitivity to anti-viral agents or reduced interactivity to an antibody to HBV surface antigen.

The common feature linking the group of inventions resides in the elucidation of the link between reduced sensitivity to anti-HBV agents such as ADV, LMV, FTC and TFB and mutation of the nucleotide sequence encoding HBV DNA polymerase or the overlapping S gene (HBsAg). However, this is already known in the art (see Chen et al., 1999, Human hepatitis B virus mutants: significance of molecular changes, FEBS Letters, 453:237-242, and citations below), as such the claims relate to multiple inventions, *a posteriori*.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/AU03/00432

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report			Patent Family Member			
WO	200194559	AU	20008109	AU	200163672	EP 1297109
WO	200157244	AU	200131415	EP	1257661	
WO	9821317	AU	37628/97	EP	964916	US 6555311
						END OF ANNEX